

## Ca Patient's 'Unexplained' Fever Laid to Infection

Medical Tribune Report

WASHINGTON—Unsuspected and difficult to diagnose infection, often of fungal etiology, may explain "unexplained" fever in cancer patients, investigators from the Division of Infectious Diseases at Indiana University School of Medicine, Indianapolis, told the 15th Interscience Conference on Antimicrobial Agents and Chemotherapy sponsored by the American Society for Microbiology.

Important clues to the presence of infection are the type of neoplasm, the granulocyte count and clinical or laboratory abnormalities indicating specific organ involvement, they suggested.

"While many neoplasms are capable of causing fever without the presence

of infection, cancer patients often have compromised immune mechanisms, either by virtue of their disease or because of therapeutic agents used in treatment, which tend to make them more susceptible to opportunistic infections," said Dr. Friedrich C. Luft, head of the research team.

### Patient Acutely Ill

He and Drs. J. Peter Rissing, Arthur White, and Geo. F. Brooks, evaluated the causes of fever of unexplained origin (FUO) in 36 cancer patients seen during a 30-month period. Sixteen patients had lymphoma, 12 leukemia, and eight solid tumors.

Each patient met certain criteria: a diagnosis of malignant neoplasm docu-

mented prior to fever onset; fever of at least three weeks duration; fever higher than 38.3 degrees centigrade on several occasions; and an uncertain diagnosis after one week in hospital.

"These criteria served to exclude patients with fever due to self-limited viral infections and those with bacterial infections responsive to antibacterial therapy," Dr. Luft explained. "These patients were acutely ill. They had persistent fever in spite of antimicrobial therapy with combinations of antibiotics which included gentamicin, cephalothin and carbenicillin."

The research team anticipated that the majority of patients selected would prove to have fever secondary to neoplasms. "This did not occur," declared

Dr. Luft. "Minimally, 50 per cent of our patients had infections. And it was not possible to rule out the presence of infection with absolute certainty in patients who had fevers presumably due to their neoplasms."

Fungi were the cause of infection in nine of the 18 infected patients. Histoplasmosis was found in three patients, candidiasis in three and aspergillosis, systemic sporotrichosis and cryptococcal meningitis in one patient each.

"This reflects the increasing importance of fungi as a source of infection in patients with compromised body defenses," noted Dr. Luft.

Six patients had unresolved pyogenic infections, one had tuberculous pericarditis, and two had viral infections. In the 18 apparently noninfected patients, fever appeared associated with some change in the neoplasm, according to Dr. Luft. "Five of the six patients with solid tumors had noted new masses or swellings and lymphoma patients often had newly enlarged lymph nodes," he said.

While the infected and noninfected group of patients had a number of features in common, for example age and sex distribution and mean duration of fever, several distinguishing parameters were noted.

"Absolute granulocyte counts were strikingly different for the two groups," said Dr. Luft. "In infected patients, marked granulocytopenia was evident. Eleven patients in this group had absolute granulocyte counts of less than 1000/mm<sup>3</sup> and five others less than 3000/mm<sup>3</sup>."

"In contrast, few of the noninfected patients had granulocytopenia. Only one patient in this group had a granulocyte count of less than 1000/mm<sup>3</sup>."

Type of neoplasm also distinguished infected from noninfected patients, according to Dr. Luft. All 12 leukemia patients had infection.

### Morphologic Exams

Morphologic examination of biopsy or aspiration specimens, with cultures, was the most productive diagnostic measure, the research team concluded. "In infected patients, likely sites for productive biopsy procedures were clinically apparent. These included pulmonary infiltrates visible on chest roentgenograms or abnormalities detected on physical examination. There was a paucity of abnormalities indicating organ system involvement with infection in the other 18 patients."

"Regardless, physicians' diagnostic efforts should not be deterred in such patients," Dr. Luft continued. "Repeated thorough evaluations for infection are warranted."

Dr. Luft stressed, however, that diagnostic measures must be tailored to the individual cancer patient. Noting that a large number of aggressive procedures were done in the apparently noninfected patients, he said: "These patients were able to withstand major diagnostic efforts whereas the often moribund infected patients could not. In the latter instances, the physician and patient together must decide whether surgical diagnostic procedures and potentially toxic antimicrobial therapy will prolong useful life or make dying difficult."

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**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or over-sedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, leukopenia, periodic blood counts and liver function tests advisable during long-term therapy.

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Med Trib 41

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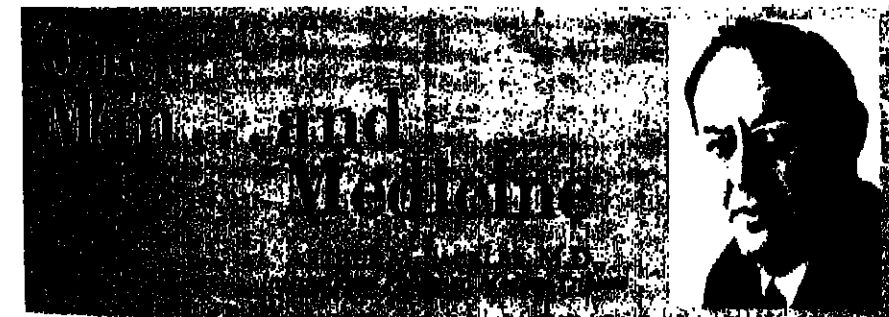
world news of medicine and its practice—fast, accurate, complete

Wednesday, November 19, 1975

## The President Catches Cold...



...and Recovers Uneventfully, a sequence of clinical events that has a particular moral for practicing physicians. Please see Dr. Sackler's column below and Dr. Lasagna's letter on treatment of colds in the adjacent columns.



## The Common and Not-So-Common Cold

I SHOULD HAVE DONE SOMETHING about this before.

Last year, in fact more than a year ago, I received a letter from an expert whose expertise and judgments have always been, for me, a source of respect and admiration—Louis Lasagna, Professor of Pharmacology, University of Rochester School of Medicine and Dentistry. Of all subjects, it was on the "common cold." I must plead guilty to failing to act sooner on his communication. I do not now, and will try to make up for my default. In exculpation of my guilt, I have asked the editor of MEDICAL TRIBUNE to publish his letter in several issues. You will find Dr. Lasagna's communication in the adjacent columns.

## President Ford Catches Cold

This was news. Ron Nessen, the White House Press Secretary, issued statements; the wire services buzzed; radio, TV and newspapers throughout the country carried the reports.

The nation was "assured" (that word was used again and again) that it was only a "head cold." According to the *New York Times*, "Mr. Nessen assured reporters the President was suffering from nothing more serious than the lingering effects of a head cold Mr. Ford has been trying to shake."

Clearly it was not pneumonia.

The *Times* continued, quoting the President's spokesman, "It's just not possible to tell how long it will take him to recover from the cold."

Clearly, it was not pneumonia.

We were informed, "The illness was a common cold."

## Meditation

### ...Without Metaphysics

Before you plunk down \$125 for a course in transcendental meditation, try the simple, no cost, "non-cultic" relaxation technique devised by Drs. Herbert Benson, Sidney Alexander and Charles L. Feldman of Boston's Harvard Medical School and Beth Israel Hospital and the Worcester Polytechnic Institute in Worcester, Mass. Although the technique has not been broadly applied, the authors reported in *Lancet* (August 30) that it "seemed to decrease the frequency of P.V.C.s in most patients."

Continued on page 14

## HEW Considering Network of Centers For Amniocentesis

By FRANCES GOODNIGHT  
Medical Tribune Staff

WASHINGTON, D.C.—The first full-scale prospective study of amniocentesis performed for prenatal diagnosis has shown that the procedure is both safe and accurate, according to a summary of results made public here by the National Institute of Child Health and Human Development which sponsored the research.

The findings, based on second-trimester amniocentesis, are being reported in the *New England Journal of Medicine*.

## Dr. Lasagna Writes on Colds and Antibiotics

March 27, 1974

Dear Arthur:

One of the most constantly raised points in the current discussion about overprescribing of drugs is the alleged prescribing at a spinal reflex level of antibiotics for "the common cold." It is repeatedly said that in surveys of doctors in practice, a very high percentage of patients who come to the doctor's office for "the common cold" receive an antibiotic.

On the face of it, this seems reprehensible. On reflection, however, it occurs to me that most patients do not visit a doctor's office, and pay good money, for advice about uncomplicated coryza. I suspect, instead, that most patients with upper respiratory complaints go to see doctors suffering from a combination of cough, stuffed nose, post-nasal drip, swollen glands in the neck, earache, etc.—in other words, from secondary bacterial complications of the common cold. If this is the case, then the prescribing of an antibiotic is not wrong; rather, the question is only: what antibiotic would be best?

I ask that you print this letter in *Medical Tribune* to solicit from your readers some facts bearing on the statements I have just made. If I am wrong, then the doctors of this country deserve the severe criticism they are receiving from many quarters at present. If I am right, then the doctors are practicing good medicine, and it is the critics who deserve disapproval.

Louis Lasagna, M.D.



## Abnormal Erythrocyte Aging Found in Preleukemic State

Medical Tribune Report

CHICAGO—A prospective study of the preleukemic phase of myelomonocytic leukemia in 270 suspected patients at the Mayo Clinic has revealed a number of previously unreported findings in 33 patients who later progressed to overt acute nonlymphocytic leukemia.

Dr. Robert V. Pierre, who began the study in 1968, said the most striking new feature in bone-marrow studies of the preleukemic phase in these patients was "abnormal erythrocytic maturation, specifically megaloblastoid maturation."

Dr. Pierre, who is Associate Professor of Internal Medicine and Labora-

tory Medicine at the Mayo Clinic and Hospital, Rochester, Minn., reported his findings to a joint meeting here of the American Society of Clinical Pathologists and the College of American Pathologists.

Atypical megakaryocytic morphology in the bone marrow was also common in the 33 patients, he noted, as well as "abnormal granulopoiesis with left-shifted maturation and a slight increase in blasts, nuclear cytoplasmic maturation dissociation, and monocytoid features." Marrow hypoplasia was also much more common than previously reported, Dr. Pierre said.

Patients in the Mayo study were entered on the basis of "unexplained cytopenias or other combinations of findings described in previous studies as suggestive of preleukemia."

Myelomonocytic leukemia, he explained, is a nonlymphocytic acute leukemic process involving all of the myeloid cell lines. The very frequent monocytic appearance of the granulocyte is another characteristic of the overt phase.

Of the 270 patients originally involved, only 131 are still living. In addition to the 33 who did develop leukemia, four "suspects" have become normal, seven developed "a characteristic chronic myeloproliferative syndrome, in particular, agnogenic myeloid metaplasia," and 19 have cytogenetic abnormalities.

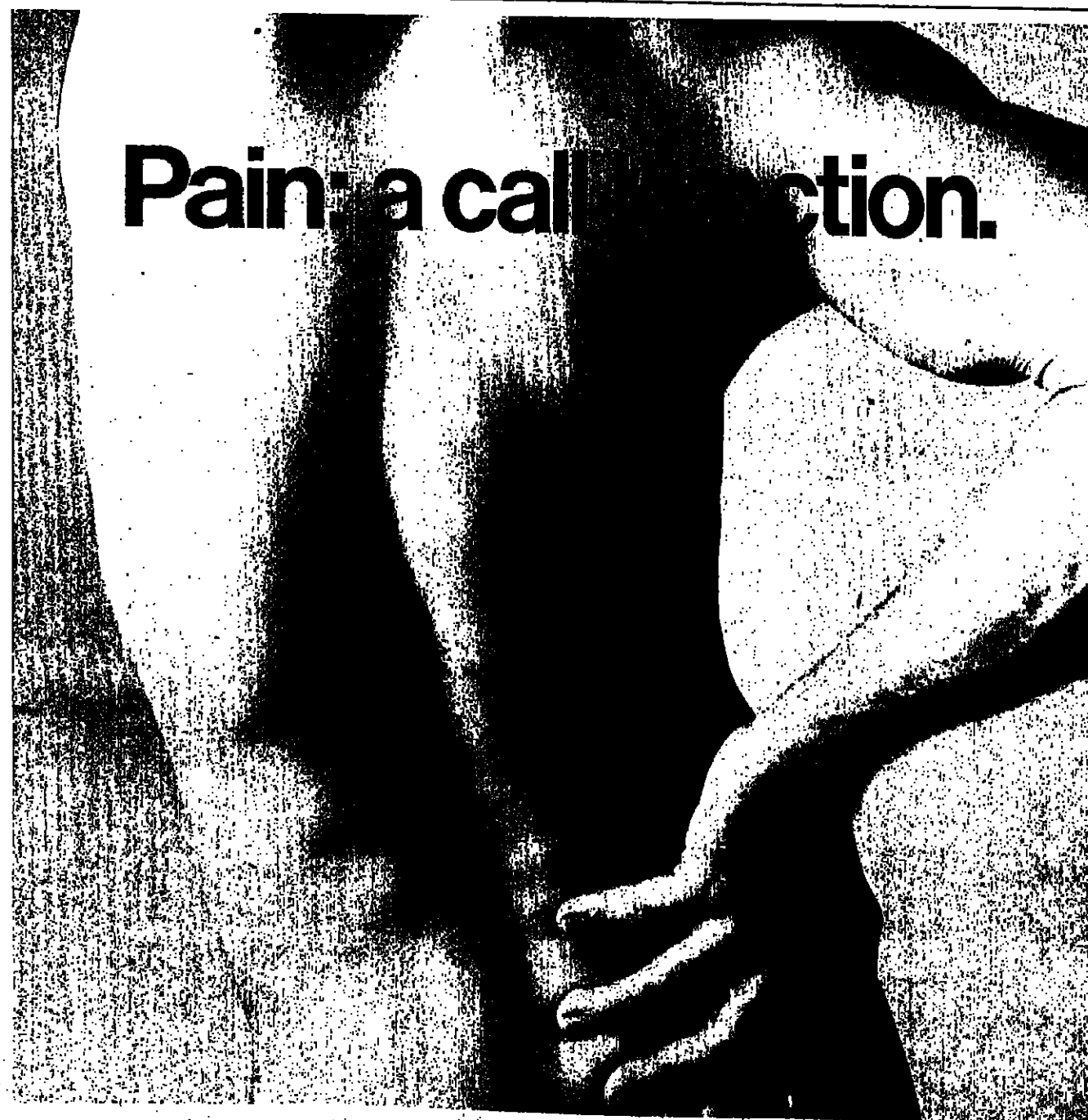
Besides the new findings, the study

strongly indicated that suspected patients who show cytogenetic abnormalities "have an extremely poor prognosis, even if acute leukemia does not supervene," Dr. Pierre commented.

Hematologic findings included anemia in all 33 patients, leukopenia in 18, thrombocytopenia in one third of the patients, and a combination of immature granulocytes and nucleated red cells in 13, Dr. Pierre said.

### Most Common Abnormality

The most common abnormality in red blood cell morphology was oval macrocytosis, he noted. "In addition to the preponderance of patients with macrocytic anemias [not due to B-12 or folate deficiency], an additional seven patients had dimorphic peripheral blood pictures with oval macrocytes and hypochromic microcytic red cells."



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Usage in Ambulatory Patients. Oxycodone may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. The patient using Percodan should be cautioned accordingly.

Interactions with Other Central Nervous System Depressants. Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, other tranquilizers, sedative hypnotics or other CNS depressants (including alcohol) concurrently with Percodan may exhibit an additive CNS depression. When such combined therapy is contemplated, the dose of one or both agents should be reduced.

Usage in Pregnancy. Safe use in pregnancy has not been established relative to possible adverse effects on fetal development. Therefore, Percodan should not be used in pregnant women unless, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Usage in Children. Percodan should not be administered to children.

Salicylates should be used with caution in the presence of peptic ulcer or coagulation abnormalities.

PRECAUTIONS: Read injury and increased intracranial pressure. The respiratory depressant effects of narcotic analgesics may be exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

Ataxic abdominal conditions. The administration of Percodan or other narcotics may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

Special risk patients. Percodan should be given with caution to certain patients such as the elderly or debilitated, and those with severe impairment of hepatic or renal function, hypotension, Addison's disease, and prostatic hypertrophy or urethral stricture.

Phenacetin has been reported to damage the kidneys when taken in excessive amounts for a long time.

ADVERSE REACTIONS: The most frequently observed adverse reactions include light-headedness, dizziness, pallor, nausea and vomiting. Some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation and pruritus.

DOSEAGE AND ADMINISTRATION: Dosage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed the usual dosage recommended below in case of more severe pain or in those patients who become tolerant to the analgesic effect of narcotics. The usual adult dose is one tablet every six hours as needed for pain.

DRUG INTERACTIONS: The CNS depressant effect of Percodan may be additive with that of other CNS depressants. See WARNINGS.

Aspirin may enhance the effect of sedatives and inhibit the effect of salicylate antagonists.

MANAGEMENT OF OVERDOSEAGE: Signs and Symptoms: Serious overdose with Percodan is characterized by respiratory depression, extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdosage, apnea, circulatory collapse, cardiac arrest and death may occur. The ingestion of very large amounts of Percodan may, in addition, result in acute salicylate intoxication.

First Aid: Primary attention should be given to the establishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist, naloxone, hydrochloride, when specifically indicated, may be used to reverse depression which may result from overdose or unusual sensitivity to oxycodone, including euphoria. Therefore, an appropriate dose of one of these antagonists should be administered, preferably by the intravenous route, immediately with effect of respiratory resuscitation. Since the duration of action of oxycodone may exceed that of the antagonist, the patient should be kept under continued surveillance and repeated doses of the antagonist should be administered as needed to maintain adequate respiration.

An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression.

Respiratory, circulatory and other supportive measures should be employed as indicated.

gastric emptying may be useful in removing unabsorbed drug.

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See facing page for Brief Summary.

\*See dosage and administration section of Brief Summary.

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## One Man...and Medicine

ARTHUR M. SACKLER, M.D.  
International Publisher, Medical Tribune



### The Common and Not-So-Common Cold

Continued from page 1

the first of Mr. Ford's Presidency, and White House officials sought to provide assurance that it was minor."

Let us now seek to reconstruct the case from reliable press sources. The Chicago Tribune Press Service noted that "Ford had been coughing for about a week, Nessen said, before he telephoned Dr. William Lukash, his personal physician, Sunday afternoon." President Ford played two sets of tennis Sunday afternoon and then took a nap. Nessen said, "His cold was worse when he awoke, so he called Lukash and asked him to stop by after dinner."

Dr. Lukash did so. He "noted the fever and added an antibiotic to his prescribed medical regimen, which had included a nasal spray and cough medicine, Lukash, a Navy rear admiral, also suggested that the President sleep late Monday and curtail his activities." This was done.

By Monday White House Press Secretary Ron Nessen said, "Overall, the President is feeling reasonably well except for sinus congestion, a tendency to cough, and a temperature slightly above 100 degrees."

The President's recovery apparently has been uneventful since then. There have been no reported antibiotic side effects, such as sensitivity reaction, development of resistant organisms, etc. He simply recovered and returned to work.

### Prescription for the President

Now, let us take another look... one of the most powerful men in the world was sick. What to do? What was done was reported... the President of the United States was given an antibiotic for his cough, a nasal spray presumably for sinus congestion, and great heavens—an antibiotic for his respiratory tract infection, reassuredly not for pneumonia. Apparently the President's physician acted like the good physician he is. Probably the only thing additional we would have done would have been to put him on a regimen of high dosages of Vitamin C.

But just a moment! Was the organism cultured? What was found? We were reassured that it was a "head cold"—no reported identification of a specific bacterial infection. From the sequence of events it appears that the physician to the President of the United States acted like most competent practicing physicians—not like an "armchair medical general" far from the scene of patients' homes or physicians' offices, far from clinic or hospital.

### Questions Needing Answers

What will happen now? Will the President's physician be open to censure by a PSRO committee? Where were the experts from our Communicable Disease Center? Where were our

F.D.A. officials? What will the effect of Dr. Lukash's actions be on his malpractice premiums? Is President Ford's physician now open to a potential malpractice suit because he may have defied the injunctions of F.D.A. officials, package inserts and assorted experts?

It would appear that Professor Louis Lasagna in his 1974 communication was right in his suspicion that "most patients with upper respiratory complaints go to see doctors suffering from a combination of cough, stuffed nose,

## For Cervical Dysplasia in Fertile Women: Cryosurgery

Medical Tribune Report

PHILADELPHIA—The use of cryosurgery in management of young women with dysplasia of the cervix who want to retain their childbearing potential was advocated here at a National Conference on Gynecological Cancer held by the American Cancer Society.

Dr. Paul B. Underwood, Jr., of the Medical University of South Carolina, said no serious complications had occurred in 64 patients receiving this treatment on an outpatient basis after combined investigation by colposcopy and biopsy had shown noninvasive cervical epithelial atypically.

Of the group, 29 have been followed for more than a year post-surgery and all but two of the 29 have continued to maintain negative cervical cytology when examined at three-month intervals, Dr. Underwood reported.

The women represented a sizable percentage of the 317 patients who have been referred to the university's colposcopy clinic because of an abnormal Pap smear since the establishment of the clinic late in 1972.

### Visualization Important

Those considered for cryosurgery included 73 women desirous of having a child (or additional children) as well as one elderly woman whose medical condition precluded surgery. In 10 cases, however, colposcopic examination was believed inadequate because the endocervical canal could not be visualized fully, and these women were treated by cold knife conization.

Dr. Underwood stressed the importance of adequate visualization of the endocervix, specifically of the upper border of the lesion. He also warned against reliance on colposcopy alone to classify the degree of dysplasia.

"It cannot be overemphasized," he said, "that colposcopy must be combined with biopsies of the exo- and endocervix before attempting cryosurgery."

Management of the 64 patients included a repeat Pap smear, colposcopy,

post-nasal drip, swollen glands in the neck, earache, etc.—in other words, from secondary bacterial complications of the common cold."

I think that Professor Lasagna is deserving of the replies he seeks from physicians in the practice of medicine whom he addressed at the end of his letter:

"I ask that you print this letter in MEDICAL TRIBUNE to solicit from your readers some facts bearing on the statements I have just made. If I am wrong, then the doctors of this country deserve the severe criticism they are receiving from many quarters at present. If I am right, then the doctors are practicing good medicine, and it is the critics who deserve disapproval."

Until we hear from you, out there, may I close with a heartfelt observation:

What's good enough for the President of the United States is good enough for our patients, the citizens of the United States.

and then cryosurgery using the double-freeze technique with a refrigerant of Freon or nitrous oxide. All patients were treated on an outpatient basis without analgesia or anesthesia and none required discontinuance of the procedure because of pain.

### 'Far More Economical'

Patients were kept in the supine position for 10 minutes and then permitted to dress and resume normal activities. They were told to wear either an external or internal pad, and advised to abstain from intercourse for 10 days.

Such treatment is "far more economical" than therapy by cold knife conization, Dr. Underwood pointed out. At his institution, charges for cryosurgery have been \$35 compared to an approximate cost of more than \$730 (covering the two days of hospitalization, anesthesia charges, physician's fee, etc.) incurred for the cone procedure.

The gynecologist said that questions have been raised about therapy of mild dysplasia, since many women regress to normal without treatment. But, he continued, findings from a number of studies indicate that the majority do not, and many progress to more serious atypicalities.

For this reason, and because the term "abnormal Pap smear" has such disturbing connotations for patients, Dr. Underwood believes a benign procedure such as cryosurgery is advisable even though the recurrence rate of dysplasia in treated women can be expected to increase with the length of follow-up.

### Meningococcal Vaccines

Medical Tribune Report

CINCINNATI—Meningococcal group A and C polysaccharide vaccines are now being manufactured here by Merrell-National Laboratories under F.D.A. licensure. At present, the vaccines are destined only for military personnel or other adults at high risk.

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CLINICAL NEWS NOTE: "Our studies indicate that the major impediment to the successful reversal of vasectomy is the quality of the reanastomosis and that a non-strictured vasovasostomy can only be accomplished with confidence by microsurgical operating techniques." (Dr. Sherman J. Silber, Assistant Professor of Urology, University of California School of Medicine, San Francisco. See page 1.)

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880 Third Avenue, New York, N.Y. 10022

Telephone: 421-4000

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### WARNINGS

Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte imbalance may precipitate hepatic coma. Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.

Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported. Use in Pregnancy: Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

### Neonatal Mothers

Thiazides cross the placental barrier and appear in cord blood and breast milk.

### PRECAUTIONS

Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hypotension, hyponatremia, hypokalemia, and hypocalcemia). Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Worsening of weakness, lassitude, muscle pain or cramps, dizziness, restlessness, muscle pain or cramps, and gastrointestinal disturbance such as nausea or vomiting.

Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk, long-term administration of a diuretic or ACTH. Interference with adequate oral intake of electrolytes may also contribute to hypokalemia. Digitalis toxicity is especially with reference to myocardial activity.

Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt, except in rare instances when the hy-

ponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.

Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration. Thiazide drugs may increase the responsiveness of the antihypertensive effects of the patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.

If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.

Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

### ADVERSE REACTIONS

Gastrointestinal—Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, Central Nervous System—dizziness, vertigo, parosmia, headache, xanthopsia, Dermal—rash, urticaria, necrotizing angitis, Stevens-Johnson syndrome, and other hypersensitivity reactions.

Hematologic—leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, Cardiovascular—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Other—hyperglycemia, glycosuria, hyperuricemia, muscle aches, weakness, restlessness, vitamin adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

### DOSAGE

Individualize dosage by titrating for maximum therapeutic response at the lowest possible dose. Hypertension—Initial—Usual dose 75 mg daily. Maintenance—After a week dosage may be adjusted downward to as little as 25 mg or upward to as much as 100 mg daily. Combined therapy to be added gradually and with caution because of the potentiating effect of this drug. Dosages of parenteral diuretics should be halved.

Edema—Initial—25 to 100 mg daily for several days. Maintenance—25 to 100 mg daily or intermittently. Refractory patients may require up to 200 mg daily.

SUPPLIED: Tablets, 50 mg (yellow, scored); bottles of 30, 60, 100, 1000, 5000, and Accu-pak blister units of 100, 1000, 25 mg (pink, scored); bottles of 30, 60, 100 and 5000.

Consult complete literature before prescribing. CIBA Pharmaceutical Company, Division of CIBA-GEIGY Corporation, Summit, New Jersey 07901.

CIBA

Wednesday, November 19, 1975

MEDICAL TRIBUNE

5

## Infection Control

### Interhospital Spread of Gram-Negatives a Potential Threat

By ANASTASIA TOUFEXIS  
Medical Tribune Staff

WASHINGTON—Interhospital spread should be considered a potential source of nosocomial gram-negative rod infections, Dr. Dennis R. Schaberg, of the Center for Disease Control (CDC) in Atlanta, advised members of the 15th Interscience Conference on Antimicrobial Agents and Chemotherapy sponsored here by the American Society for Microbiology.

"Interhospital spread has been recognized in the past as a serious cause of infection, especially of gram-positive *Staphylococcus aureus*," Dr. Schaberg told MEDICAL TRIBUNE. "However, it has not been recognized as often for gram-negative organisms and is perhaps more common than we think. But the potential for spread is there. These pathogens can be carried from hospital to hospital by transferred patients or by personnel common to many facilities."

Dr. Schaberg, a member of CDC's Bureau of Epidemiology, was called in, for example, to investigate an outbreak of *Serratia marcescens* in a Nashville, Tenn. hospital. A preliminary review revealed that the outbreak had initially occurred at another facility, Dr. Schaberg said. Before the field investigation was completed, the infection had spread to two more hospitals.

*Serratia marcescens*, a pathogen which seems to occur only in hospitalized, compromised patients, has been recognized over the last ten years as a serious, if uncommon, cause of infection and often death, he said.

#### Four Hospitals Involved

"Between April 1973 and December 1974, 210 patients in four geographically separate hospitals in Nashville were infected with *Serratia marcescens* resistant to all currently available parenteral antibiotics," Dr. Schaberg told the meeting, speaking for Drs. Walter B. Stamm, Robert A. Alford, William Schaffner and John V. Bennett of the CDC and the V.A. Hospital and Vanderbilt University School of Medicine in Nashville. "Twenty-one patients had bacteremia and there were eight infection-related deaths."

"Actually, we were rather lucky, if I can use that word, that the organism was so resistant," Dr. Schaberg told MEDICAL TRIBUNE. "Too often, interhospital spread of gram-negative organisms goes unnoticed. But we noticed this one right away because the pathogen was so unusual."

The initial outbreak occurred in April 1973 in the large intensive care area of one facility, said Dr. Schaberg in recapitulating the progress of the epidemic. "A total of 18 patients were infected. In all except one, the infection was of the urinary tract and catheter associated. The outbreak lasted through June 1973."



A fourth hospital reported infections in five patients in one intensive care unit in December of 1974.

"The serotype (O1:H7) and phage type (186) of the epidemic strain were identical in all four hospitals, with background *Serratia* strains yielding a variety of other serotypes," Dr. Schaberg noted.

#### Identifying the Source

In trying to identify a common source, the investigators first looked for a single medication, solution or device, but found none. "Then we looked for a patient transferred from one hospital to another," said Dr. Schaberg. "This remains a possibility although we were

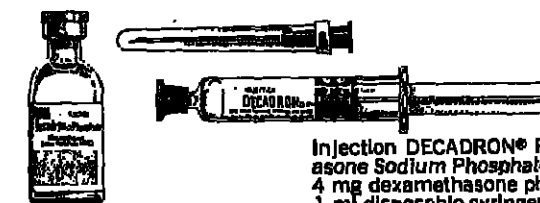
unable to find confirming evidence.

"However, we did recover the organism from the hands of personnel, a large number of whom were common to the four hospitals. This suggested passive carriage as the mode of transmission between hospitals."

Infected patients were treated either with amikacin, a new experimental drug, or a synergistic combination of colistin and trimethoprim sulfa, said Dr. Schaberg. "Infection has been eliminated from two hospitals and the number of infections in the other two has decreased."

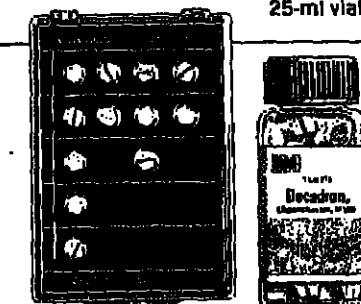
"But in the absence of truly effective therapy, prevention must be stressed," Dr. Schaberg declared. "This involves better catheter care, handwashing and aseptic technique. And also more restricted use of broad spectrum antimicrobial therapy."

## INJECTABLE



Injection DECADRON® Phosphate (Dexamethasone Sodium Phosphate) (MSD) equivalent to 4 mg dexamethasone phosphate per ml, in 1-ml disposable syringes and 1-ml, 5-ml, and 25-ml vials.

## INGESTIBLE



Tablets DECADRON® (Dexamethasone) (MSD) 0.75 mg, in bottles of 100 and 5-12 PAK® (package of 12).

## BREATHABLE



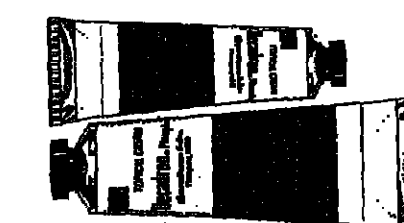
RESPIHALER® Phosphate (Dexamethasone Sodium Phosphate) (MSD) containing per metered spray, dexamethasone sodium phosphate equivalent to approximately 0.1 mg dexamethasone phosphate or 0.084 mg dexamethasone, fluorochlorohydrocarbons as propellants, and alcohol 2%, in 12.5-g cartridge delivering at least 170 sprays and refill cartridge.

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Sterile Ophthalmic Solution DECADRON® Phosphate (Dexamethasone Sodium Phosphate) (MSD) 0.1% equivalent to 1 mg dexamethasone phosphate per ml, in 5-ml OCHIMETER® OPHTHALMIC DISPENSER and 2.5-ml and 5-ml dropper bottles.

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Topical Cream DECADRON® Phosphate (Dexamethasone Sodium Phosphate) (MSD) 0.1% equivalent to 1 mg dexamethasone phosphate per gram, in 15-g and 30-g tubes.

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... brief summaries of editorials or comments in current medical and scientific journals.

### Focus on Hepatitis

Although the recent advances in viral hepatitis are heartening, they also bring into sharper focus a new problem. The new tests for HAV [hepatitis A virus], combined now with various tests for detection of HBV [hepatitis B virus] infection, have afforded substantiation of the claims that a high proportion of transfusion-associated hepatitis is caused by as yet unidentified infectious agents, neither HAV nor HBV. Feinstone and co-workers recently studied 22 patients each of whom had an episode of transfusion-associated hepatitis negative for HBS Ag [hepatitis B surface antigen], HBC Ag [hepatitis B core antigen] and the respective antibodies to these antigens. Antibody response to HAV was measured by immune electron microscopy. None of the 22 patients developed serologic evidence of HAV infection. Whether such unidentified infectious agents are also important causes of hepatitis in human populations at large will require much study. Nevertheless, it is evident that the more is learned about viral hepatitis the more appears to remain unknown." (*Editorial, Shalom Z. Hirschman, M.D., West. J. Med. 123:224, Sept., 1973*).

### Surgical Learning...

... Another current phenomenon in surgical learning in community hospitals might be called the "residency crisis." (After a number of years of preparation and warning, the disapproval of surgical residency training in many community hospitals seems to be under way.) It is quite apparent that free-standing community hospital surgical residency programs, that is, those without strong medical school affiliations, will soon become extinct. ...

... Survival of a community hospital residency in the immediate future will require, in addition to the absolute sine qua non of meaningful medical school affiliation, 1) a full-time director, 2) demonstrable ability to attract American trainees, 3) clear evidence that resident learning (as opposed to resident service) is the focus of the program, and 4) regular documentation of specialty board certification by graduates of the program. Not all of these requirements are, at present, part of the written policy of residency approval bodies, but they seem nonetheless obvious. Nor is it difficult to defend them. Those community hospitals in which the issue of the future of the surgical residency still exists must decide... whether they can and should meet these requirements. ...

"Stamford Hospital surgeons have found themselves very much involved in the issues touched upon here, and we cannot claim to have solved them. We are trying to learn from others. We hope that our progress in learning will reflect favorably on our profession and on the care of our patients." (*Editorial, Gerald O. Strauch, M.D., Conn. Med. 39:343, Sept., 1973*).

# ...patient acceptance of the drug [guanethidine] is actually as great as it is with methyldopa...

1. Langford HG: Hypertension, in Conn HF (ed): *Current Therapy*. Philadelphia, The WB Saunders Co, 1973, p 201.

when hypertension threatens to outrun control

To encourage patient compliance: convenient once-a-day dosage

Convenient once-a-day dosage is an important factor in patient acceptance of Ismelin.

But more important is its effectiveness. In so many cases, substituting or adding a little Ismelin may provide the extra measure of hypertensive control needed. In a falling rauwolfia-thiazide regimen, for example. Or if tolerance develops to methyldopa.

Perhaps the most effective anti-hypertensive ever available, Ismelin usually brings blood pressure down to stay. And tolerance is rare.

Used in conjunction with thiazides, which "...augment the antipressor activity of more potent agents, including...guanethidine..." the

required addition may be small.

Whenever Ismelin is added to other antihypertensives, initial doses should be small, and increased gradually by small increments. Once control is established, all drug dosages should be reduced to the lowest effective level, often minimizing side effects.

Patients should be warned about the potential hazards of orthostatic hypotension and cautioned to avoid sudden or prolonged standing or exercise.

It may require a little extra patient cooperation.

But may well be worth it—for the extra protection Ismelin offers against uncontrolled hypertension.

References: 1. Langford HG: Hypertension, in Conn HF (ed): *Current Therapy*. Philadelphia, The WB Saunders Co, 1973, p 201. 2. Langford HG: Drugs for arterial hypertension. *N Engl J Med* 1973; 289:1073-1075. 3. *Medicine*, 52:1073-1075, 1973.

Ismelin® sulfate (guanethidine sulfate)

INDICATIONS: Moderate and severe hypertension either alone or as an adjunct. CONTRAINDICATIONS: Known or suspected pheochromocytoma; hypersensitivity to guanethidine; severe heart failure not due to hypertension; patients taking MAO inhibitors.

WARNING: Ismelin is a potent drug and can lead to disturbing and serious clinical problems if used without proper precautions. Physicians should be familiar with its effects and its use before prescribing, and patients should be warned not to deviate from instructions.

Warn patients about the potential hazard of orthostatic hypotension, which can occur frequently and is most marked in the morning. It is accentuated by hot weather, alcohol, and is accompanied by lightheadedness, weakness, and loss of consciousness. To help prevent falling, advise patients to sit or lie down with head of bed raised and legs lowered. Advise patients to avoid sudden or prolonged standing or exercise while taking the drug.

Concurrent use with meprobamate derivatives may cause excessive postural hypotension, bradycardia, and mental depression.

## First Month Found 'Critical Period' in Patient Compliance

Medical Tribune Report

DALLAS, TEX.—A study of patient compliance in 89 persons with ocular hypertension has indicated that the decision to treat strongly influences compliant behavior, and that the first month after initial diagnosis is "the critical period" in determining compliance or noncompliance.

Reporting to the American Academy of Ophthalmology and Otolaryngology here, Dr. John F. Bigger, Associate Professor of Ophthalmology at the Medical College of Georgia, Augusta, said 37 patients (33 per cent) were lost during the 12-to-20 month follow-up. Of these, 26 dropped out within one month of diagnosis.

Patients were selected on the basis of "intraocular pressure of 22 mm Hg or higher, with asymptomatic ocular pressure abnormalities." The 20 patients with glaucomatous visual field defects and 21 of the remaining 69 with normal visual fields were treated, he said; the remaining 48 went untreated. Records were then studied about one year later to determine how many patients were maintaining regular follow-up.

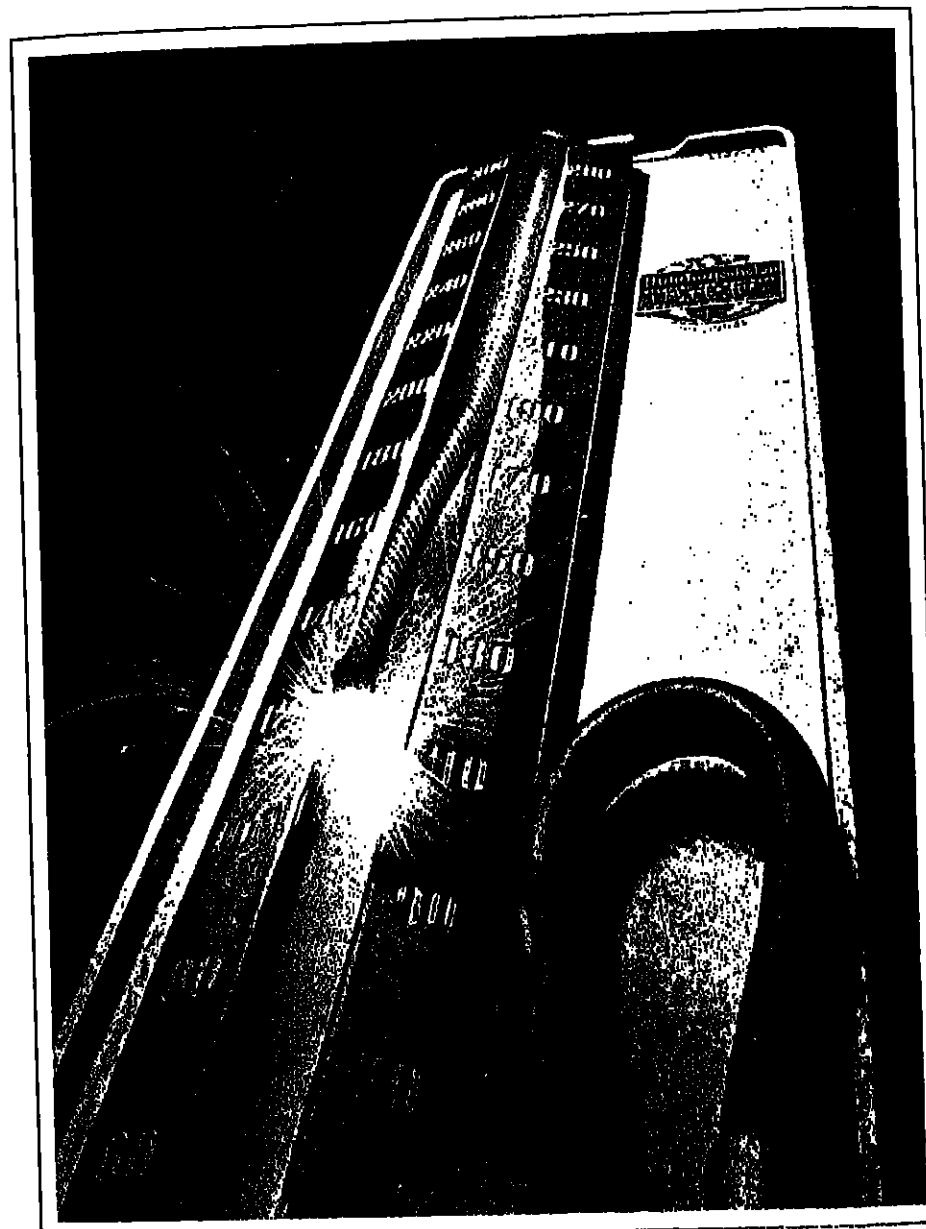
### Treated Groups Rate Better

"Compliance rates were almost identical in the two treated groups [i.e., three dropouts in each group], and were 30 to 40 per cent better than the rate in the non-treated patients [i.e., 22 dropouts]," Dr. Bigger said. The study, he noted, was carried out in the suburban office of a general ophthalmology group practice.

Noncompliance is also likely to occur in cases of chronic, asymptomatic illness requiring long-term therapy, the benefit of which is not immediately apparent or is accompanied by side effects, and where discontinuing therapy causes no immediate effect, Dr. Bigger said. "In addition, the illness itself may also diminish the patient's capacity to comply."

Dr. Bigger also noted that, in general, the more a therapeutic regimen

Continued on page 17



add a little **Ismelin® sulfate** (guanethidine sulfate)

...because the goal is 140/90

If possible, withdraw therapy 2 weeks prior to surgery to reduce the possibility of vascular collapse and cardiac arrest during anesthesia. If emergency surgery is indicated, administer pressor and anesthetic agents cautiously in reduced dosage and have oxygen, atropine, vasopressors, and IV solutions ready for immediate use to treat vascular collapse. Vasopressors should be used with extreme caution in patients on Ismelin because of the possibility of augmented response and the greater propensity for cardiac arrhythmias.

Dosage requirements may be reduced in presence of fever. Exercise special care when treating patients with a history of bronchial asthma, since their condition may be aggravated. Use in Pregnancy: The safety of Ismelin for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient. PRECAUTIONS: The effects of guanethidine are cumulative over long periods; initial dose should be small and increased gradually in small increments. Use very cautiously in hypertensive patients with renal disease and with retention of fluid. Do not give Ismelin to patients with severe cardiac failure except with extreme caution. In incident cardiac decompensation weight gain

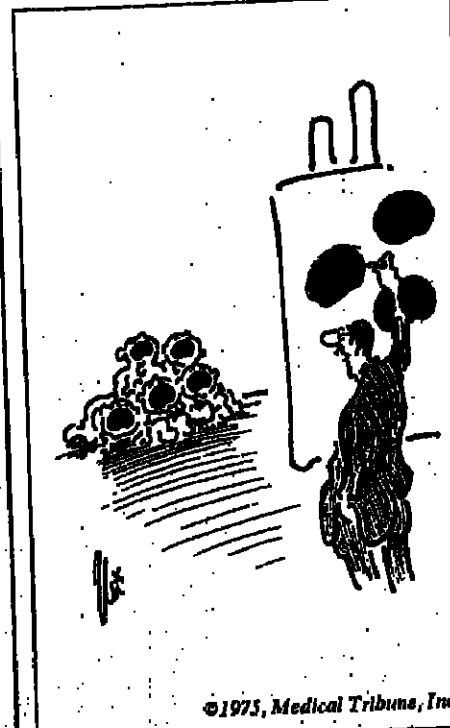
or edema may be averted by the administration of a diuretic. Remember that both digitalis and Ismelin slow the heart rate.

Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone. Amphetamine-like compounds, stimulants (eg, ephedrine, methylphenidate), tricyclic antidepressants (eg, amitriptyline, imipramine, desipramine), and other psychopharmacologic agents (eg, phenothiazines and related compounds), and oral contraceptives may reduce the hypotensive effect of guanethidine. Discontinue MAO inhibitors for at least one week before starting Ismelin.

ADVERSE REACTIONS: Frequent reactions due to sympathetic blockade—dizziness, weakness, lassitude, syncope. Frequent reactions due to unopposed parasympathetic activity—bradycardia, increase in bowel movements, diarrhea may be severe and necessitate discontinuance of the drug. Other common reactions—inhibition of ejaculation, fluid retention, edema, congestive heart failure. Other less common reactions—dyspnea, fatigue, nausea, vomiting, nocturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, paresthesias, blurring of vision, parotid enlargement, myalgia, muscle tremor, mental depression, chest pains (anginal), chest paresthesias, nasal congestion, weight gain, and asthma in susceptible individuals. Although a causal relationship has not been established, a few instances of anemia, thrombocytopenia and leukopenia have been reported.

DOSAGE AND ADMINISTRATION: Initial dosage should be low and increased gradually by small increments. Before starting therapy, consult complete product literature. HOW SUPPLIED: Tablets, 10 mg (pale yellow, scored) and 25 mg (white, scored); bottles of 30, 60, 100 and 1000.

CIBA Pharmaceutical Company, Division of CIBA-GEIGY Corporation, Summit, New Jersey 07901



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C I B A

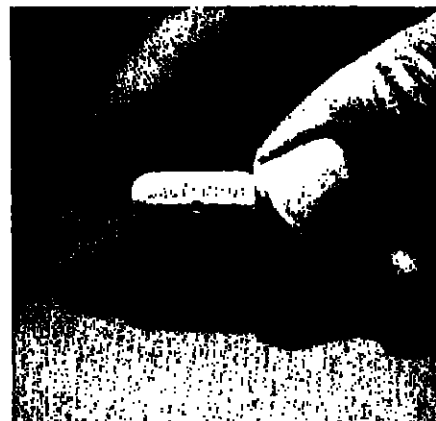
# Roche introduces new Bactrim DS

Each tablet contains 160 mg trimethoprim and 800 mg sulfamethoxazole.

## double strength tablets

## only 1 tablet b.i.d. for better patient compliance

For chronic or frequently recurrent urinary tract infection.



### Just 1 tablet b.i.d.

When the patient with chronic or frequently recurrent urinary tract infection fails to comply with therapy, persistent bacteriuria or relapse may occur. Single tablet b.i.d. dosage makes compliance easier.

### Same efficacy with half the number of tablets

Studies have established bio-equivalency of Bactrim DS double strength tablets with the Bactrim single strength tablets.

### Greater economy for patients

Fewer tablets per day offer sufficient medication for the full course of therapy at a lower cost to the patient.

Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** Chronic urinary tract infections evidenced by persistent bacteriuria (asymptomatic or symptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris* and *Proteus morganii*.

**NOTE:** The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method (Federal Register, 37:20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Bactrim therapy. If infection is confined to the urine, "Intermediate susceptibility" also indicates a likely response. "Resistant" indicates that response is unlikely.

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

**Warnings:** Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hemopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. Data are insufficient to recommend use in infants and children under 12.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid

intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, anorexia, abdominal pains, hepatitis, diarrhea and pancreatitis. **CNS reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tremor, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, parotiditis, nodules and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

**Dosage:** Not recommended for children under 12. Usual adult dosage: 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) every 24 hours
Below 15	Use not recommended

**Supplied:** Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100; Tel-E-Dose® packages of 100. Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Packs of 40, available singly and in trays of 10. Oral suspension, containing in each teaspoonful (5 ml) the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole; fruit-licorice flavored—bottles of 16 oz (1 pint).

## new Bactrim DS double strength tablets

(160 mg trimethoprim and 800 mg sulfamethoxazole)

For chronic cystitis and pyelonephritis evidenced by persistent bacteriuria and due to susceptible organisms

ROCHE Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

Wednesday, November 19, 1975

MEDICAL TRIBUNE

### Current Opinion

## On the Crisis of Access

By DR. STANLEY S. BERGEN, JR.  
President  
College of Medicine and Dentistry of New Jersey

[The following comments have been excerpted from a keynote address by Dr. Bergen at a recent Colloquium on Primary Care, "Understanding Tomorrow's Medicine Today," held in Newark—Ed.]

HERBERT FILL IN A RECENT MONOGRAPH has noted, "The true concept of cure has been lost. More and more people do not live healthier lives; they are merely prevented from dying. There is indeed a technical but no human conception of what health is." He feels that we are "self-defeating" by our "single-minded insistence on purely external solutions." He is obviously urging a broader rather than fragmented approach to total health and the well-being of the whole person. Medical and/or mental care cannot be separate from health care—environment, life style and personal responsibility for the maintenance of health and prevention of illness.

Political leaders, health economists, practicing physicians, medical educators, the lay public—all have been able to identify the problems of the delivery of health care. Comedians joke about the inaccessibility of physicians on Wednesday afternoons or weekends. The idolized TV physician is available to millions of viewers and yet, his counterpart cannot be identified in most cities of our country.

During the 1950's and 1960's, the trend in medical education was towards specialty orientation. This orientation took place initially in the large medical centers where the expansion of knowledge required that individual specialty practitioners be available in order to adequately address the issues of acute in-hospital care. Physicians began grouping in multi-specialty groups so that a one-stop location could be provided for the full spectrum of health care needs of a large community. Hospitals ascended as the focal point for the delivery of health care and the emphasis within medical schools was upon educational programs that were categorically developed and specialty oriented. Funding from the National Institutes of Health and other federal programs encouraged the development of the specialty programs... while the emphasis upon general practice and generalists seemed to diminish.

### Manpower Distribution

Janeway compared Great Britain and the United States concerning the distribution of physician manpower between general practitioners and specialists... The ratios are... 1 specialist for every 2.75 general practitioners in the United Kingdom, and 4 to 1 in the United States.

With cost of health care rising rapidly, Janeway notes that the impact of such physician distribution affects the cost. In 1970 each individual in the United Kingdom spent an average of \$107.00 on medical services while in the United States during the same period these services cost \$390.00. The cost per practicing physician in the United States, therefore becomes \$286,740.00.

We are all aware of the tremendous inflation of health care cost between 1960-1975. During this period, expenditures for health increased from \$26

billion to over \$104 billion annually while public expenditures for health care rose from \$6.4 billion to \$41.3 billion. The health industry increased from 2.5 million workers in 1960 to almost 5 million in 1974. Last year, the health industry provided over 1 billion physician and dentist visits and over 30 million short-term hospital services.

### Increased Ambulatory Care

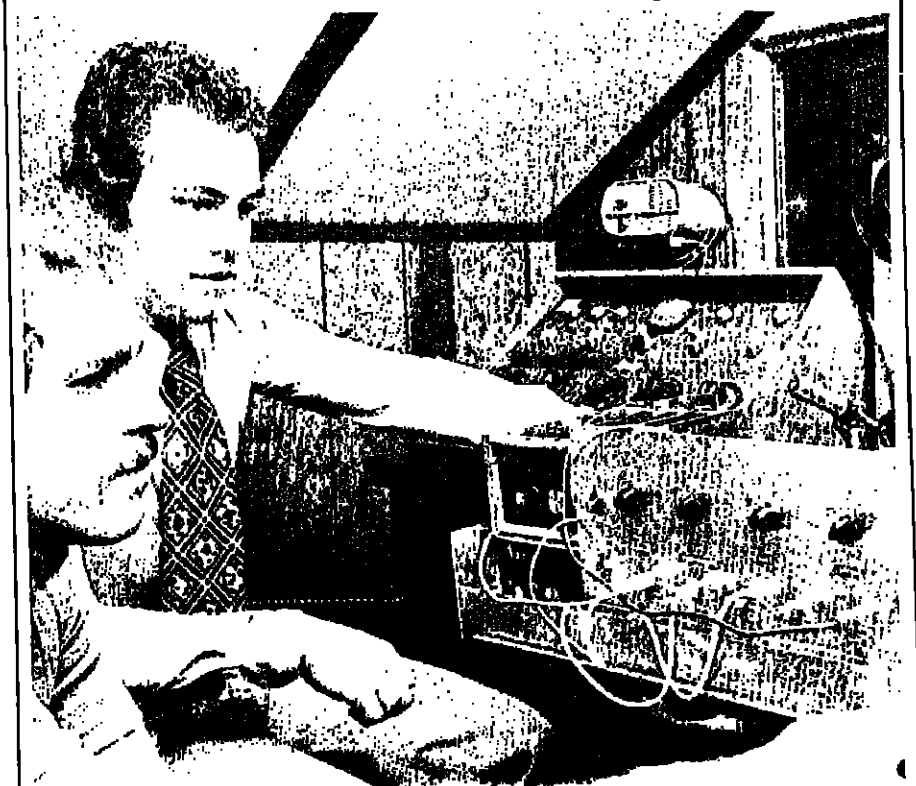
With the loss of primary care physicians from the cities, the number of ambulatory care and out-patient visits has grown from 223 to 562 per thousand population in the 20-year period from 1947-1967. In 1953, there were two out-patient visits for each in-patient admission while by 1967, the ratio had increased [to] 4 to 1. Many of these visits were provided by hospital clinics and similar structured facilities which often are unable to provide for an established patient-doctor relationship.

Despite the tremendous increase in health care expenditures over the last few years, there has been little evidence of improvement in the crude death rate in the United States or significant changes in the major causes of death. The major impact has come from public health measures, improved prevention and an awareness of the impact of various social issues on health rather than improved medical care for the masses. Yet... disproportionate funds are spent on illness vs. health maintenance and prevention.

Therefore, although our problems may seem to be access to facilities, personnel and financing, it may well be that the primary problem is one of access to adequate information.

Something has happened to our approach to the health care in the United States. While I would be the last to suggest that we return to the inadequate, ill-prepared and by today's standards, poorly educated general practitioner of the 1900's, it may be important for us to return to an era of willingness to care. We have probably entered an era in which dramatic medical advances that benefit many will be few and far between except possibly in cancer. The growth of applicable medical knowledge may plateau despite continued exciting advances in scientific biomedical knowledge. It behooves all medical practitioners, medical bureaucrats, public health officials and health professions educators to join in formulating the plan by which all citizens will have access to health care and become recipients of the benefits of medical knowledge gleaned for research of recent decades. All citizens must be provided with the information needed for sharing the responsibility for a healthy nation.

### Aid for Sensorineural Hearing Impairment



New type hearing aid for those with sensorineural hearing impairment selectively amplifies consonants but not vowels, unlike conventional aids which simply amplify sounds. Adjusting feasibility model they developed are audiologist Paul Yanick, right, himself a sufferer from impaired hearing, and electronic engineering professor Harris Drucker, of Monmouth (N.J.) College.

We may have avoided one of the main problems of ethics facing the medical profession in the future, that is, the question of the accessibility of our patients to health information and the willingness that we express in sharing such information with our patients despite the fact that the sharing of this information may exert a significant impact on the patterns of health care, the traditional doctor/patient relationship and the economics of the profession and industry. Franz Ingelfinger has urged that medical ethicists and physicians communicate more closely with each other on problems of medicine and medical practice. I would add the need to include the public in such discussions because I believe the central issue of health ethics today is access to information. Not merely the "right to know" concept concerning what has been done for a patient, the diagnosis, prognosis and options but also what role the patients can and should play in their own health care. There is no doubt that professionals must continue to make the primary decisions towards the care of individual patients and decisions concerning those options available to the patient in the delivery of health care. However, we must no longer make these decisions alone but rather must listen to the needs as expressed by our patients and citizens.

### Symptom Not the Disease

Society's decision-making can be effected by the professional but only if society is well informed of its choices and the effect that these choices may have on other options and other areas requiring fiscal, personnel and natural resources.

I believe that the apparent lack of adequate primary health care is a symptom and not the disease. We have neither shared with the public the decision making process, the allocation of resources and the determination of priorities nor have we provided the infor-

mation necessary for the public to assume a role in the decision making process and take responsibility for a measure of their own health care, health maintenance and improved well-being. Actually, if correctly used, we may have adequate health care potential. Unfortunately, the patient has been overwhelmed by the emphasis on the quality of care received from the specialists and the professional has been impressed with status, finances, hospital privileges, etc., factors which have forced issues in the opposite direction. We have created a two-class system in the United States: the rich vs. the poor, the hospital vs. ambulatory care, primary care vs. specialty care and the informed vs. the uninformed.

### System Must Change

Financial incentives, educational systems, patterns of behavior and expectations all must be changed for, at present, they work against the provision of general health care for all our citizens. They all favor decisions which virtually preclude good primary care, maximum hospital usage, short hospitalization, appropriate physician visits and delegation of responsibility to non-physicians. All physicians must return to a posture of caring for people rather than one of providing care alone.

In the context of team health care, I can imagine that different types of physician providers may function effectively as long as they maintain equal status, access to hospitals and patients. The specialists, the generalists and the physician extenders should all be part of the effort to provide the health care system with adequate, competent professionals. Each should function upon a level of equal status as part of the total effort. Primary care must become an accepted part of the comprehensive delivery system, act as the resource of

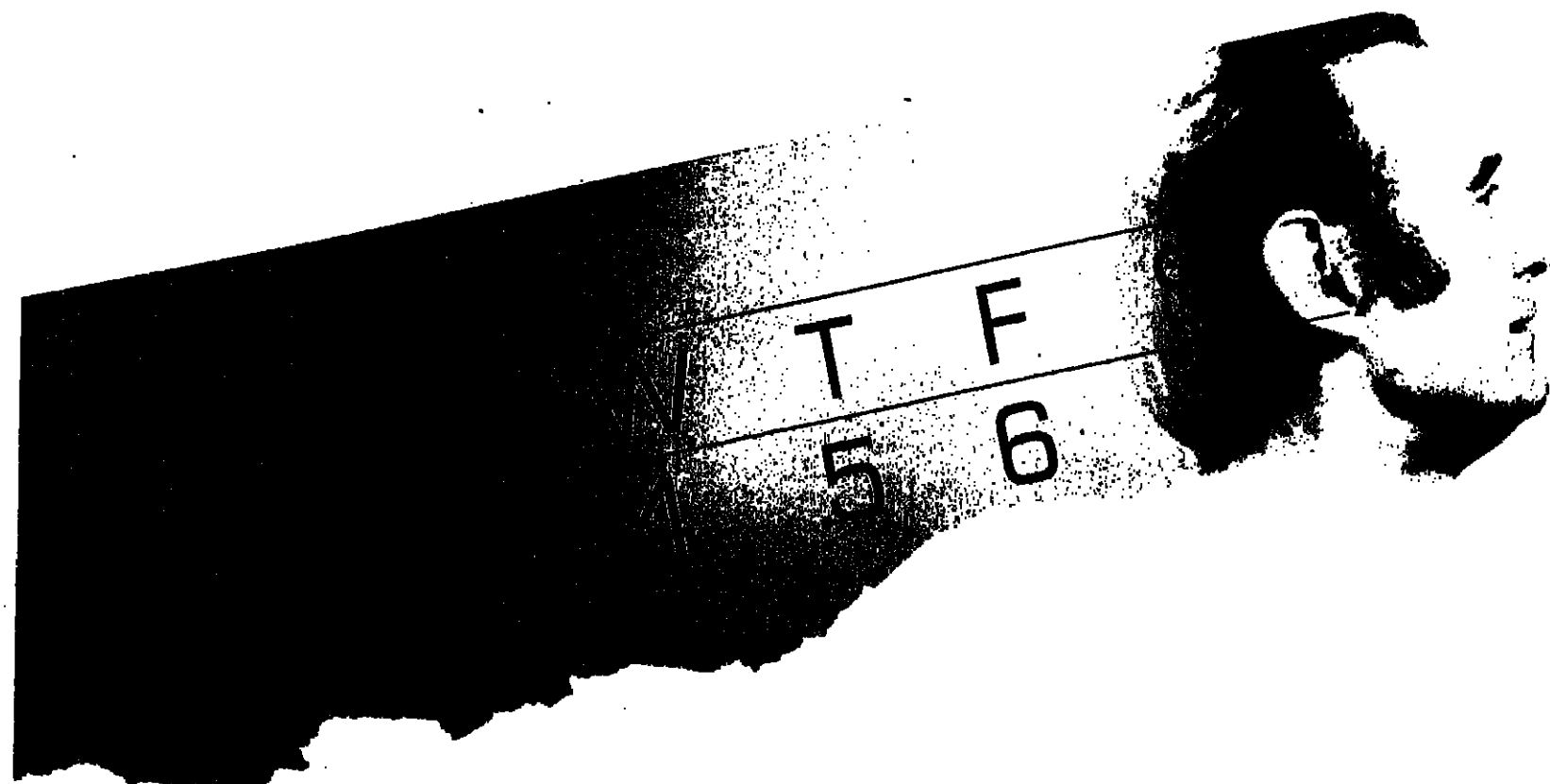
Continued on page 15



# MELLARIL® (THIORIDAZINE)

TABLETS: 10 mg, 15 mg, and 25 mg thioridazine HCl, U.S.P.

## IN CLINICALLY SIGNIFICANT DEPRESSIVE NEUROSIS— RESULTS OFTEN SEEN IN A WEEK



Mellaril can often help you give patients with depressive neurosis relief within a week. In 14 double-blind studies of four weeks duration, 339 patients with depressive neurosis received Mellaril. In these studies, 55% of the overall improvement was observed by the end of the first week, and a total of 293 patients (86%) improved during the four weeks.\*

With Mellaril, patients often have an end to such symptoms as insomnia, G.I. symptoms, irritability, dejection, and hopelessness before they have a chance to become entrenched.

\*Data on file at Sandoz Pharmaceuticals.

### Mellaril (thioridazine) short-term therapy of moderate to marked depression with variable degrees of anxiety in patients with depressive neurosis

Before prescribing or administering, see Sandoz literature for full product information. The following is a brief summary.  
**Contraindications:** Severe central nervous system depression, comatose states from any cause, hypertensive or hypotensive heart disease of extreme degree.  
**Warnings:** Administer cautiously to patients who have previously exhibited hypersensitivity reactions (e.g., blood dyscrasias, jaundice) to phenothiazines. Phenothiazines are capable of potentiating central nervous system depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorus trichloride; carefully consider benefit versus risk in less severe disorders. During pregnancy, administer only when the potential benefits exceed the possible risks to mother and fetus.  
**Precautions:** There have been infrequent reports of leukopenia and/or agranulocytosis and convulsive seizures in epileptic patients; anticonvulsant medication should also be maintained. Pigmentary retinopathy observed primarily in patients receiving larger than recommended doses, is characterized by discoloration of the fundus, brownish coloring of the iris, and impairment of night vision; the possibility of its occurrence may be reduced by remaining within recommended dosage limits. Administer cautiously to patients participating in activities requiring complete mental alertness (e.g., driving), and in females than in males. Do not use epinephrine in treating drug-induced hypotension since phenothiazines may induce a reversed adrenergic effect on occasion. Daily doses in excess of 300 mg should be used only in severe neuropsychiatric conditions.  
**Adverse Reactions:** Central Nervous System—Drowsiness, especially with large doses, dizziness in treatment; infrequently, pseudo-parkinsonism and other extrapyramidal symptoms; rarely, nocturnal

confusion, hyperactivity, lethargy, psychotic reactions, restlessness, and headache. Autonomic Nervous System—Dryness of mouth, nose, and throat, constipation, nausea, vomiting, diarrhea, nasal stuffiness, amenorrhea, inhibition of ejaculation, and peripheral edema. Skin—Dermatitis and skin eruptions of the urticarial type, photosensitivity. Cardiovascular System—ECG changes (see Cardiovascular Effects below). Other—Rare cases described as parotid swelling. The following reactions have occurred with phenothiazines and should be considered: **Autonomic Reactions**—Mydriasis, orthostatic hypotension, anorexia, paralytic ileus, **Cutaneous Reactions**—Erythema, exfoliative dermatitis, contact dermatitis, **Blood Dyscrasias**—Leukopenia, leukopenia, eosinophilia, thrombocytopenia, agranulocytosis, pancytopenia, **Allergic Reactions**—Fever, laryngeal edema, anaphylactic shock, asthma, **Hepatic Toxicity**—Jaundice, biliary stasis, **Cardiovascular Effects**—Changes in terminal portion of electrocardiogram, including prolongation of Q-T interval, lowering of T-wave, and appearance of a wave tentatively identified as a bifid T or a U wave have been observed with phenothiazines, including Mellaril (thioridazine); these appear to be reversible and due to altered repolarization, not myocardial damage. While there is no evidence of a causal relationship between these changes and significant disturbance of cardiac rhythm, several sudden and unexpected deaths apparently due to cardiac arrest have occurred while taking the drug. While proposed, periodic electrocardiograms are not regarded as predictive. Hypotension, rarely resulting in cardiac arrest. **Extrapyramidal Symptoms**—Akathisia, agitation, motor restlessness, dystonic reactions, trismus, torticollis, opisthotonus, oculogyric crises, tremor, muscular rigidity, and akinesia. **Persistent**

**Tardive Dyskinesia**—Persistent and sometimes irreversible tardive dyskinesia, characterized by rhythmic involuntary movements of the tongue, face, mouth, or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements) and sometimes of extremities may occur on long-term therapy or after discontinuation of therapy, the risk being greater in elderly patients on high-dose therapy, especially females; if symptoms appear, discontinue all antipsychotic agents. Syndrome may be masked if treatment is reinstituted, dosage is increased, or antipsychotic agent is switched. Fine vermicular movements of tongue may be an early sign, and syndrome may not develop if medication is stopped at that time. **Endocrine Disturbances**—Menstrual irregularities, altered libido, gynecosmia, lactation, weight gain, edema, false positive pregnancy tests. **Urinary Disturbances**—Retention, incontinence. **Other**—Hyperreflexia, behavioral effects suggestive of a paradoxical reaction, including excitement, bizarre dreams, aggravation of psychosis, and toxic confusional states; following long-term treatment, a peculiar skin-eye syndrome marked by progressive pigmentation of skin or conjunctiva and/or accompanied by discoloration of exposed sclera and cornea; stellate or irregular opacities of anterior lens and cornea; systemic lupus erythematosus-like syndrome. **Dosage:** Dosage must be individualized according to the degree of mental and emotional disturbance, and the smallest effective dosage should be determined for each patient. In adults with depressive neurosis the usual starting dosage is 25 mg i.i.d. or q.i.d. and the dosage ranges from 10 mg i.i.d. to q.i.d. for more severely disturbed patients; the total daily dose ranges from 20 mg to a maximum of 200 mg. **SANDOZ PHARMACEUTICALS, EAST HANOVER, NEW JERSEY 07930**

Wednesday, November 19, 1975

MEDICAL TRIBUNE

11

The Only Independent Weekly Medical Newspaper in the U.S.

## Medical Tribune

and Medical News  
Published by Medical Tribune, Inc.

### In Medicineland, U.S.A.

*Child of the pure unclouded brow  
And dreaming eyes of wonder!  
Though time be fleet, and I and thou  
Are half a life asunder,  
Thy loving smile will surely hail  
The love-gift of a fairy-tale.*

DEAR ALICE:

I have another wondrous fairy-tale to tell. In our country we have a special bureau to regulate drugs. They decide which drugs the doctor may have and which drugs he may not have. They also decide which drugs may be used without the doctor's prescription and which, because of their potency or problems in their use, require a doctor's prescription.

Now, Alice, you may begin to understand some of my confusions in our medical wonderland here. For years this bureau, the Food and Drug Administration, has fought to have essential food elements such as vitamins declared as food at one dosage level and as a drug at another. Our courts decided they could not do this with the vitamins found in oranges, lemons and limes. But verily they are able to require a prescription for another vitamin, vitamin A, when it is to be taken in an amount equal to or even less than what is provided in a slice of liver.

Recently I visited in Washington and in my naivete I inquired as to recent changes in the package insert instruc-

tions for doctors in the most potent drug used to lower the sugar in the blood of those who have too much—we call them diabetics. It was recently up-dated, I was told. Being of simple faith, I went out and bought some packages of this potent substance—insulin. To my astonishment, there was no doctor's package insert with the usual warnings of side effects, contraindications, none of the official basic and background information required for drugs too potent to be bought without a prescription.

Now, insulin can cause coma and can kill. In fact, until recent advances, it could kill without leaving a trace. But the requirement set for vitamin A prescription is deemed to be unnecessary for insulin. Anyone can buy it over-the-counter. Ah, I thought, perhaps it is because it is an old drug. No. Perhaps it is because it is so essential and is used so frequently by patients. No. Digitalis is an old drug and digitalis is a life-saving drug, and it may be used for a lifetime, but digitalis requires a prescription.

My head reels. Of course, consistency is the hobgoblin of little minds. Why the difference, dear? Well, *Thy loving smile will surely hale To see how "Wonderland's" rules are made.*

A.M.S.

### Restraints...and Scientific Inquiry

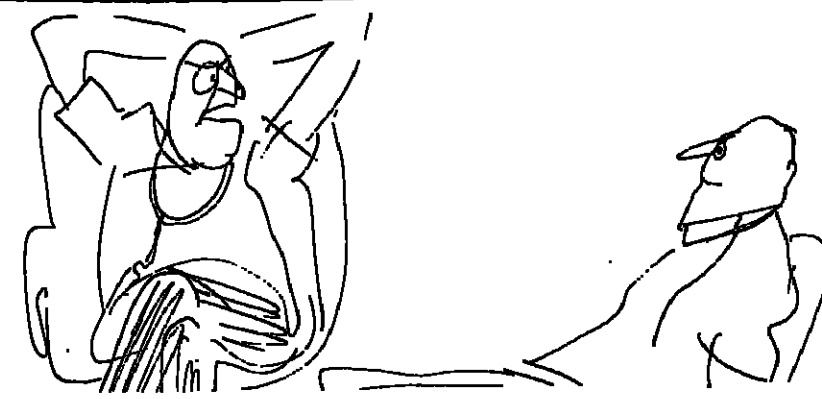
TWO MONTHS AGO, a thoughtful and balanced editorial on "Freedom of Inquiry" appeared in an issue of *Science*. The author, Dr. DeWitt Stetten, Jr., Deputy Director of Science at N.I.H., pointed out that the first amendment to the Constitution "explicitly forbids the Congress from abridging the freedoms of speech and the press," yet abridgement does occur, from time to time, "subject to the test of a real and present danger."

Dr. Stetten observed that freedom of inquiry is of importance comparable to that of speech and the press. Curtailing the freedom of inquiry has proved disastrous in past and present historical periods. Anxieties—and more than that—have been voiced currently about inquiries into the genetic contributions to intelligence; experiments that may be performed on informed adults, on minors, on fetuses, and on prisoners; screening infants for genetic defects; interference in human conception, as by "artificial insemination, abortion, cloning, in vitro fertilization or the use of surrogate mothers;" genetic engineering. Dr. Stetten suggests that in these and like problems "we treat freedom of inquiry as we have learned to

treat freedom of speech—that is, agree to abstain when there is a real and present danger." The dangers he refers to are those to "the community, the environment, or the individual."

The editorial evoked responses agreeing and disagreeing with Dr. Stetten. It is apparent that there are scientists who find it difficult to accept any limits to the absolute right of free inquiry. Such a viewpoint was expressed by a few investigators quite vehemently at the International Asilomar conference convened last February to consider the hazards of genetic manipulation by recombinant DNA molecules. But the conference did more or less define what was considered permissible and what was not by drawing up a list of recommended precautions to be taken by investigators working in the field of genetic engineering.

If investigators demand an unrestricted right to the freedom of inquiry, they must act with responsible self-restraint in the interest of society. Scientists must be sensitive to real and present dangers to the community, the environment and the individual—and must also point out when such dangers are truly not present.



"You know what I say when they say 'What's up, Doc?'  
I say, 'None of your goddamn business!'"

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### A Service in Malpractice

I read with dismay the comments of Dr. Sidney A. Bernstein (MT, Sept. 24). Dr. Bernstein accused me and my service of contributing to the malpractice problem. This allegation arose from a foundation of ignorance for Dr. Bernstein has no understanding of the nature and function of our organization, nor did he bother to inquire.

National Medical Advisory Service is a physician-run screening panel designed to evaluate medical liability cases for defense and plaintiff attorneys. Fifty per cent of our cases come from defense council. Very often we can successfully assist our colleagues; at times we cannot. At least 60 per cent of the cases which we evaluate for plaintiffs are determined to be without merit. We have been remarkably successful in dissuading prosecution in those cases. This is our most valuable function. Without a service such as ours the medically naive attorney will grope aimlessly, file suit needlessly and be driven underground into the arms of the few unscrupulous medical people of whom we are all aware. Lawyers need competent advice if this trend is to be stopped. Our introductory letter, which Dr. Bernstein found distasteful, is one way to alert the attorney that competent medical advisors are available.

I am afraid that it is those physicians who recoil at the word "malpractice" and hide when a lawyer calls who have most fueled this problem. Plaintiffs and their attorneys have no medical expertise. We well-trained, ethical physicians must willingly review their problems if we are to return fairness to medical litigation.

RONALD E. GOTS, M.D., Ph.D.  
Medical Director  
National Medical Advisory Service  
Washington, D.C.

### Fetal Music

Please accept my thanks and congratulations on Dr. Sackler's series [on von Karajan in] "One Man . . . and Medicine." Being a member of Los Angeles Doctors Symphony Orchestra, I am very sensitive to the tranquilizing effects of classical music.

I wonder how you feel about our rock and roll with its noise pollution over ninety decibels. It has been my experience, though limited, that the music of Brahms, especially the First Symphony, closely resembles the pulsations found in the intrauterine environment of the fetus.

May I suggest, perhaps, that an entire symphony could be written based entirely on the flow of energy, fluid and neuromuscular movement of the human body. Has this ever been done? It would of course, have to include the Neonate and his struggle onto full maturity. Finally, I feel that the car radio has contributed a great deal to distractive and detached environs, causing many accidents.

A. M. GROSSMAN, M.D.  
Beverly Hills, Calif.

### Hyperlipoproteinemia

Frances Goodnight's article (MT, Oct. 15) reviewing my recent presentation before the American Chemical Society was lucid and accurate in all respects. The editorial about it, unfortunately, contained several substantive inaccuracies.

I pointed out that therapeutic responses in the homozygous form of familial hypercholesterolemia is disappointing while therapy in other forms of hypercholesterolemia is, while not totally satisfactory, rather successful. The editorial had this point reversed.

I pointed out the theoretical possibility that an agent that increased the rate of uptake of lipids into peripheral tissues—if it also increased the uptake into the arteries—might accelerate atherosclerosis while lowering plasma lipid levels. The editorial clouds the point, implying that lowering plasma lipid levels might somehow *per se* hasten the development of atherosclerotic lesions. Undoubtedly, the reverse is usually true.

I carefully pointed out that my presentation was speculative. The editorial incorrectly refers to "newly available evidence" that I cited as though it bore directly on the feasible but undemonstrated paradox I outlined. There is in fact no evidence to my knowledge that any agent currently in use or currently under investigation actually causes the kind of dissociation about which I was speculating. The evidence from cell culture studies provides a basis for speculation but it would be unfortunate if your readers were left with the impression that the probability of encountering such a dissociation is very great. It probably is not.

A reference to Frances Goodnight's piece, which provided the background and a proper perspective, was omitted from the editorial.

DANIEL STEINBERG, M.D., Ph.D.  
Professor of Medicine and Head,  
Division of Metabolic Disease  
University of California, San Diego

# An open letter to the doctors of America

Subject: The all-important physician-patient relationship

Dear Doctor:

**We must and will do something about it.**

The science and art of medicine has reached its most advanced state but the all-important physician-patient relationship is plunging to an all-time low.

**We must do something about it.**

The establishment of "cost-effective" practice rather than "therapeutic-effective" control is part of the drive towards the government's dominance, if not takeover, of medicine. Physicians personally, and the medical profession generally; medicines specifically, and diagnostic and other procedures generally, have become a target for governmental attacks as a result of the pressures generated through sensation-seeking consumerism and political expediency.

Patient regimens are too often disrupted, medical advice disregarded and medications neglected. Early diagnosis of essential conditions is being placed in jeopardy and early treatment delayed.

**We must do something about it.**

Medical Tribune has addressed these issues editorially. Medical Tribune has encouraged the mobilization of official bodies of medicine. It has reported extensively on constructive efforts by *ad hoc* committees of physicians. We have discussed these problems at great length with responsible consumer leaders, leaders in all fields of medicine, and with a whole gamut of government officials.

**More is needed.**

Medical Tribune has developed and is introducing an innovation in patient education to help rebuild and sustain the all-important physician-patient relationship. Medical Tribune has prepared a series of supplements

for use in physicians' waiting rooms, clinics, and hospitals, entitled THE GOOD DRUGS DO. Each supplement is prepared by an outstanding leader in one of the fields of medicine. Each supplement is written so that the patient can understand it. Each seeks to advance the goal of an informed patient, a cooperative patient, and a patient confident in his physician's practices, medicines and recommendations. The waiting room patient supplement, THE GOOD DRUGS DO, will be coming to you as a section of Medical Tribune.

**THE GOOD DRUGS DO patient supplement in Medical Tribune seeks to do something positive about the physician-patient relationship.**

THE GOOD DRUGS DO supplements prepared thus far consist of a general introduction by Dr. Louis Lasagna, covering the broad advance made by therapeutic medicine in the Golden Age of Therapeutics. THE GOOD DRUGS DO individual supplements then go on to take up Depression, Hypertension, Nutrition and Vitamins, Alcoholism, Diabetes, Arthritis, Psychoses, Antibiotics. Each subject supplement is prepared by an outstanding authority in the field and addressed to patients.

**Please remove THE GOOD DRUGS DO supplements from coming issues of Medical Tribune and put them in your waiting room.**

You can help us help your patients by making this essential material available to them and by advising us as to how we may make improvements in your and your patients' interests.

**We can do something about the all-important physician-patient relationship.**

Sincerely,

*Arthur W. Scheraga*  
International Publisher

## Combined Drugs Held Useful in Relief of Pain

Continued from page 24

tion or having engaged in drug abuse. Various combinations of imipramine, chlorimipramine, or trimeprazine with laevomepromazine or haloperidol were administered. Improvement was observed in 82 patients: 22 were without pain and analgesics could be discontinued, while in 60 pain was reduced and the intake of analgesics could be lowered.

Treatment had to be discontinued because of somnolence or arterial hypertension produced by laevomepromazine in 10, and urine retention in two patients due to imipramine. Haloperidol has since been substituted for laevomepromazine.

The best results were obtained in cases of postherpetic neuralgia and in lesions of the brachial and lumbosacral plexus. Generally good results were noted in patients with painful neuromyopathies, in trigeminal neuralgia, in degenerative diseases of the skeletal system (except intervertebral disc hernia), in traumatic pain of the locomotor system and in cancer.

One patient with mononeuritis multiplex, one with locomotor injuries and seven with degenerative skeletal disorders, chiefly intervertebral disc hernia, did not respond.

### Dosage Schedule

On the basis of this experience, a dosage schedule for outpatients has been worked out in which 25 mg p.o. imipramine or chlorimipramine are given three times daily with haloperidol, starting with 0.5 mg daily and carefully increased to 1 mg two to three times daily.

Inpatients are given chlorimipramine in i.v. infusions of 25-50 mg in 5 per cent glucose during two to three hours daily, shifting to 25 mg p.o. three times daily after a week, combined with haloperidol in the same dosage as received by outpatients.

If improvement is observed, the combination is continued for several weeks. Dr. Kocher said. Elderly patients should not receive more than 1.5 mg of haloperidol daily, he warned. If, as rarely happens, a Parkinson syndrome appears, an antiparkinson drug should be added.

The clinic has used this schedule in 19 patients to date, with an improvement in all but one who suffered from a degenerative disease of the skeletal system underlying a neurotic condition.

The effectiveness of the two psychotropic drugs can probably be explained by the wide-spectrum central and peripheral action they provide, Dr. Kocher said. The therapy alters the perception of pain, leading to its "depersonalization." Patients sometimes say, "I still have the pain but it no longer hurts."

The combination is also more effective in interrupting the pain-anxiety-depression-pain cycle than either thymoleptics or neuroleptics alone. One can speculate that these drugs also interfere in some way with pain-producing substances, he added.



Throngs look on in Mexico City as Danes defeat Mexico's "Aztecs" in World Women's Soccer Final.

## TRIBUNE SPORTS REPORT

### Women Effectively Engage In Rough Contact Sports

THE OLD IDEA that "frailty thy name is woman" bites the dust in these glimpses of women athletes in contact sports. As Dr. Thomas McLaughlin, Professor of Orthopedic Surgery at Case Western Reserve School of Medicine, has pointed out in an earlier issue (MT, Oct. 1, 1975), the relegation of women to the sidelines is more a cultural trend than a physiologic imperative. Apparently, women can don cleats and pads as well as men, and as Dr. McLaughlin also suggested, it's just as easy for them to break a nose or a bone or a tooth.



Collegians vie in old favorite.



They call it "sock her."



U.S. Women's karate champ Joy Turberville, defending herself.



Dallas "Bluebonnets" vs. Los Angeles "Dandelions" in pro football.



Reverse stick tackle in field hockey.



Delta Airline hostesses keep in shape with ice hockey match against the Atlanta "Embers."



## New Microsurgical Technique Reverses Most Vasectomies

Continued from page 1

anastomosis and that a non-strictured vasovasostomy can only be accomplished with confidence by microsurgical operating techniques," he stressed.

Dr. Silber, who is chief of urology at the Veterans Administration Hospital here and Assistant Professor of Urology in the University of California School of Medicine, San Francisco, reported that in the Australian trials, where the vasovasostomy has been under clinical study for four years, the procedure has been successful in 15 of the first 20 patients, a 75 per cent success rate. His own clinical trials, following three years of animal studies, were started eight months ago, and most were performed in the past five months, Dr. Silber declared. In very early fol-

low-up, two of ten patients have impregnated their wives. Dr. Silber predicted that the success rate in the American series would rise substantially with further follow-up.

### Key to Method

In the surgical method developed by himself and Dr. Earl Owen, Prince of Wales Hospital, Sydney, Dr. Silber said, the key lies in achieving an accurate mucosal approximation when reanastomosing the lumens of the transected vas deferens. Following vasectomy, he noted, the lumen of the vas distal to the ligature is about .25 to .33 mm in internal diameter, and the lumen proximal to the ligature is about .50 to .75 mm in diameter. In the vasovasostomy, performed under a dissecting microscope, a finely polished jeweler's forceps is used to dilate the lumen of the distal vas, thus creating lumens of approximately equal diameters. A mucosal anastomosis is performed, using fine nylon. Heavier sutures create the risk of sperm leakage and granuloma formation, Dr. Silber noted. A separate muscularis layer is then closed.

"This latter point is of critical importance," Dr. Silber stressed, "since a normal condition of peristalsis is essential for propulsion of the sperm from the epididymis at the time of intercourse."

He added that although "a great deal of practice is necessary to perform these micromanipulations," most surgeons can become adept after about three months of intensive training.

"Postoperative studies of the patients' semen," Dr. Silber reported, "showed no evidence of immunologic damage. Instead, it appeared that the sperm present at the time of vasovasostomy were all old and had died from autolysis. After three months, these old sperm, remnants of the previously obstructed state of the vas, were replaced by healthy spermatozoa whose genesis presumably came after successful release of obstruction. Of course, it would take three months for these new healthy sperm to appear in the ejaculate."

In an interview, he said that the duration of the vasectomy did not appear to correlate with the success or failure of the reversal procedure.

"The vasectomy of longest duration in our series was 15 years, the shortest under two years. The average time was about four or five years. The most important factor in success, we believe, is the perfect surgical anastomosis."

### Sperm Studies

He disclosed that his team is doing electron microscope sperm studies, and "our preliminary evidence suggests that, on an anatomic basis, the immunologic barrier is intact in the vasectomized male. Dr. Owen's group is doing serologic studies and thus far finds no correlation between success of the vasovasostomy and sperm antibody titer."

Dr. Silber ended on a cautionary note. However: "Our advice to any male is, don't have a vasectomy unless you're absolutely certain that you don't want it reversed. We [surgeons] can't make any guarantees. On the basis of our very early data, the best we can promise at present is a 60 per cent re-

versal rate. That figure will go up, undoubtedly, but any male contemplating a vasectomy had better remember that 100 per cent successful operations to reverse the procedure—100 per cent successful operations in anything—don't exist."

In New York, a leading authority in fertility studies said that he was not persuaded by Dr. Silber's claim that an immune response has not been shown to be a factor in the success or failure of vasovasostomies.

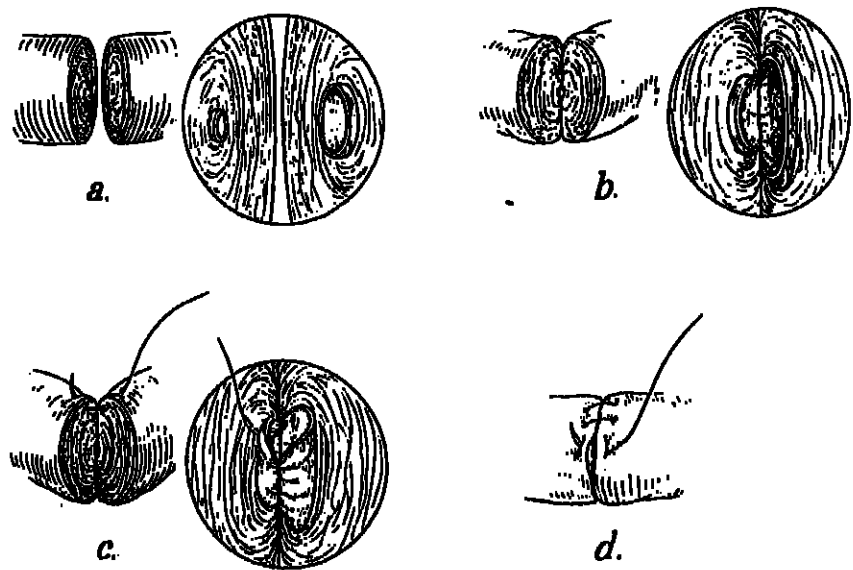
"Dr. Silber is reporting a series of 30 cases overall, a very small sampling for his conclusions," said Sidney Shulman, Ph.D., Director of the Sperm Antibody Laboratory at New York Medical College, and Research Professor of Urology and Obstetrics-Gynecology. "It is entirely possible that he may have hit on a group of patients the majority of whom don't have an immune response to the vasectomy."

"It must be remembered that a man who has sperm antibodies would not necessarily have an abnormal semen picture. The reason is that the antibodies don't meet the sperm cell until

ejaculation. If the antibody concentration is not too high, and if they're not too avid, they may react slowly and continue their reaction inside the female. That is not the kind of evidence that would show up right away or under ordinary microscope examination," Dr. Shulman continued.

### Questions Raised

Acknowledging that Dr. Silber's procedure to minimize damage to the vas deferens could make for easier sperm passage, Dr. Shulman insisted: "When he says there's no immunologic effect, I don't think he has measured it. He reports that studies under the electron microscope show no evidence of immunologic damage. I don't know what damage one would expect to see. What was the evidence that he failed to find? I would never think of using the electron microscope as a method of looking for immunologic impairment... Further, Dr. Silber hasn't cited the recent reports suggesting that a reasonable percentage of men with vasectomies do develop high titers to sperm antibodies."



Schematic presentation (above) of vasovasostomy developed by Dr. Silber shows (a) Transected ends of vas deferens seen grossly (left); in enlarged view (right) as seen under dissecting microscope, distal and proximal lumens are clearly of different diameters. (b) In enlargement, suturing of lumens has begun. (c) Transected ends of the muscularis of the vas are approximated; in microscopic view, mucosal suturing is being completed. (d) Anastomosis of the muscularis is almost complete. In photograph (below), suturing of lumens has been completed and the surgeon is about to begin final suturing of the muscularis.



### Meditation

#### ... Without Metaphysics

Continued from page 1  
tients with ischaemic heart disease."

#### The Technique

"(1) Sit quietly in a comfortable position.

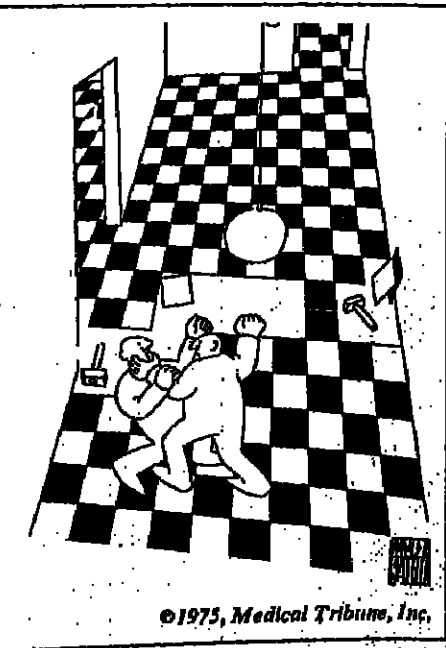
(2) Close your eyes.

(3) Deeply relax all your muscles, beginning at your feet and progressing up to your face. Keep them deeply relaxed.

(4) Breathe through your nose. Become aware of your breathing. As you breathe out, say the word "one" silently to yourself. For example, breathe in... out, "one"; in... out, "one"; etc.

(5) Continue for 20 minutes. You may open your eyes to check the time, but do not use an alarm. When you finish, sit quietly for several minutes at first with closed eyes and later with opened eyes.

(6) Do not worry about whether you are successful in achieving a deep level of relaxation. Maintain a passive attitude and permit relaxation to occur at its own pace. When distracting thoughts occur, ignore them and continue repeating "one". With practice, the response should come with little effort. Practice the technique twice daily, but not within 2 hours after any meal, since the digestive processes seem to interfere with the elicitation of anticipated changes."



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### Current Opinion

#### On the Crisis of Access

Continued from page 9

total contact, consider the patient's total needs and review the social, physical, mental and environmental impacts upon the individual. A composite solution to health problems would then evolve including imparting to the patient the information necessary to cooperate, to participate and to contribute to the individual's health care and well-being.

The crisis of access is not merely an access to health care but access to caring physicians and other health professionals and a willingness of all those professionals to provide access to information. The primary care physician of tomorrow will be a better educated,

better scientifically equipped physician who must turn considerable energy towards the counseling of the patient.

With the advent of the Health Planning Act of 1974, 93-641, there is the opportunity to develop networks of primary care facilities without the loss of specialty care located at centralized or regional hospitals. The evolution to such a system must be incremental in order to gain acceptance from both provider and consumer and invoke upon the current system, the least disruptive changes. A National Health Plan can lead to the orderly evolution of our system and provide access for all citizens to adequate health care and the expertise of providers within that

system. Education is needed on all levels of consumer programs so that we will replace fragmentation with a set of accepted and established goals and a system that unifies the health care delivery potential of our country into a mechanism that will assure access for all to facilities, professionals, financing and information.

Greater effect may come from a total system of health maintenance which includes the social, environmental and medical factors. Lelonde noted that human biology, environment and personal decisions concerning lifestyle may be as important if not more than improved medical care.

All students now in medical school must learn the multiple roles that they shall play in the future, not only as deliverers of medical care but as organizers of health care delivery programs

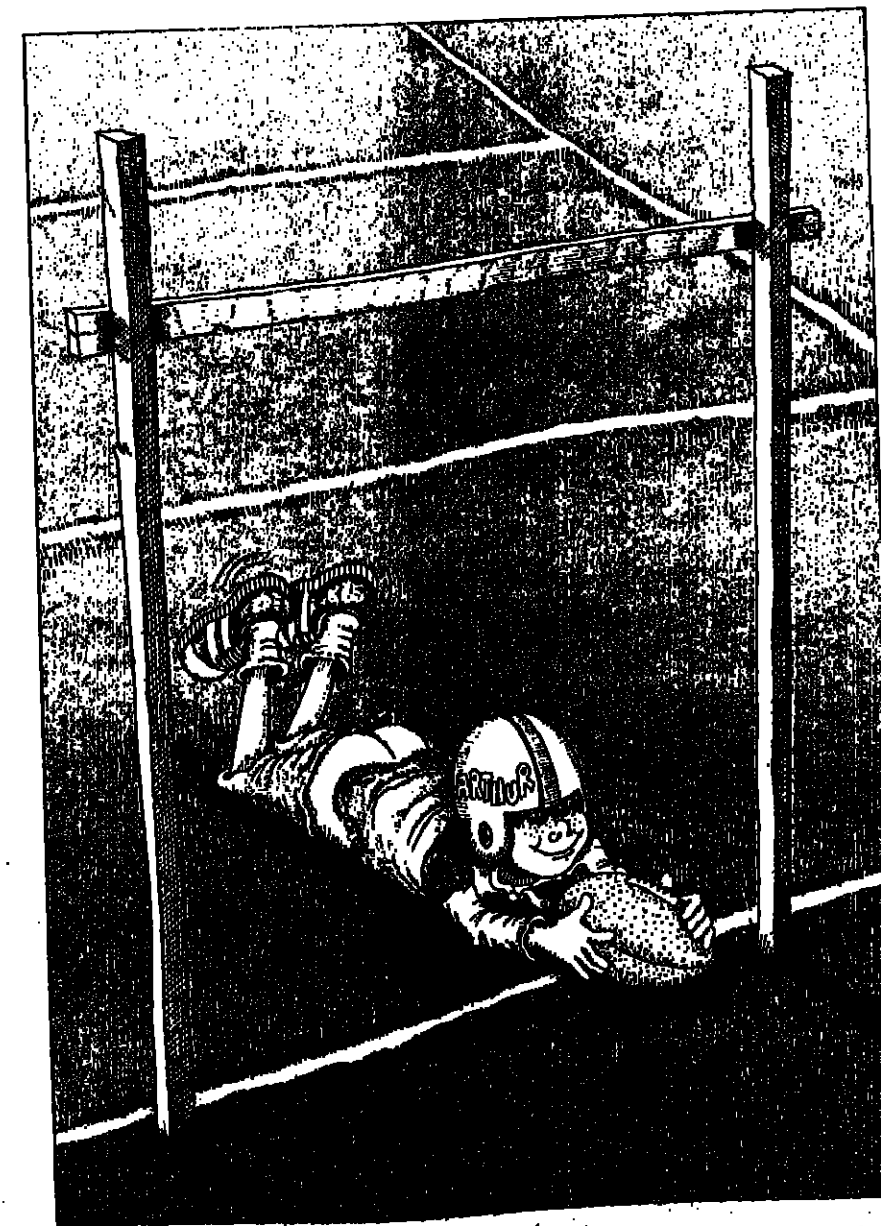
for their patients. Primary health care is a large aspect of such a program. The crisis of access is a crisis of organization, information and motivation. Health professions educators must assume the leadership role.

### Halt Baby Food Sugar?

Medical Tribune Report

WASHINGTON—Some 370 health professionals and health students have signed a petition sponsored by the Center for Science in the Public Interest, urging the F.D.A. to halt production of baby food desserts and to demand that manufacturers remove added sugar from other products. Some desserts, it was disclosed, derive 27 to 44 per cent of their calories from added sucrose. Other products are also "embarrassingly high" in added sugar, said Dr. Michael Jacobson, codirector of C.S.P.I.

# WORMS BLITZED



A single dose of Antiminth (1 cc. per 10 lbs. of body weight, 1 tsp./50 lbs.—maximum dose, 4 tsp.=20 cc.) offers highly effective control of both pinworms and roundworms.

Antiminth has been shown to be extremely well tolerated by children and adults alike in clinical studies.\* Pleasantly caramel-flavored, it is non-staining to teeth and oral mucosa on ingestion... doesn't stain stools, linen or clothing.

One prescription can economically treat the entire family.

**ROERIG**  
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Pinworms, roundworms controlled with a single, non-staining dose of

**ANTIMINTH®**  
(pyrantel pamoate)

equivalent to 50 mg. pyrantel/ml.  
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**ROERIG**  
A Division of Pfizer Pharmaceuticals  
New York, New York 10017

\*Data on file at Roerig



## Tribune Economic Analysis

Heading Off  
The Danger of  
High Oil PricesBY ELIOT JANEWAY  
Consulting Economist

The OPEC 10 per cent increase on oil (already at \$10 a barrel) will speed erosion of the entire world economy. The chance of heading off the danger hinges on America's resolution and resourcefulness in undoing OPEC's latest outrage.

Forcing the withdrawal of the 10 per cent increase will not be enough. Nothing short of a rollback to a \$7 price base—as a starter—will release the brakes now holding the economy back.

The prospect of splitting OPEC's facade of unity, and forcing price cuts out of its weaker sisters, has been discounted by some as a lost cause. But the admitted financial distress of a growing list of OPEC members is now making this a practical proposition.

Indonesia is the most attractive candidate for the role of price-cutter. Her borrowings make Iran's seem moderate. She is running six months behind on settling up her import bills and her oil isn't moving.

The American economy would get a double benefit from selecting Indonesia as the agent for splitting up OPEC. Indonesia is a major oil supplier for Japan, which has been hurt by the OPEC gouge even more than America. Japan has been restraining herself from dumping her backed-up production onto the American market. Persuading Indonesia to assure Japan that cheaper oil is coming back is one sure way to protect America's shaken industrial communities from this shock.

## Ask Janeway

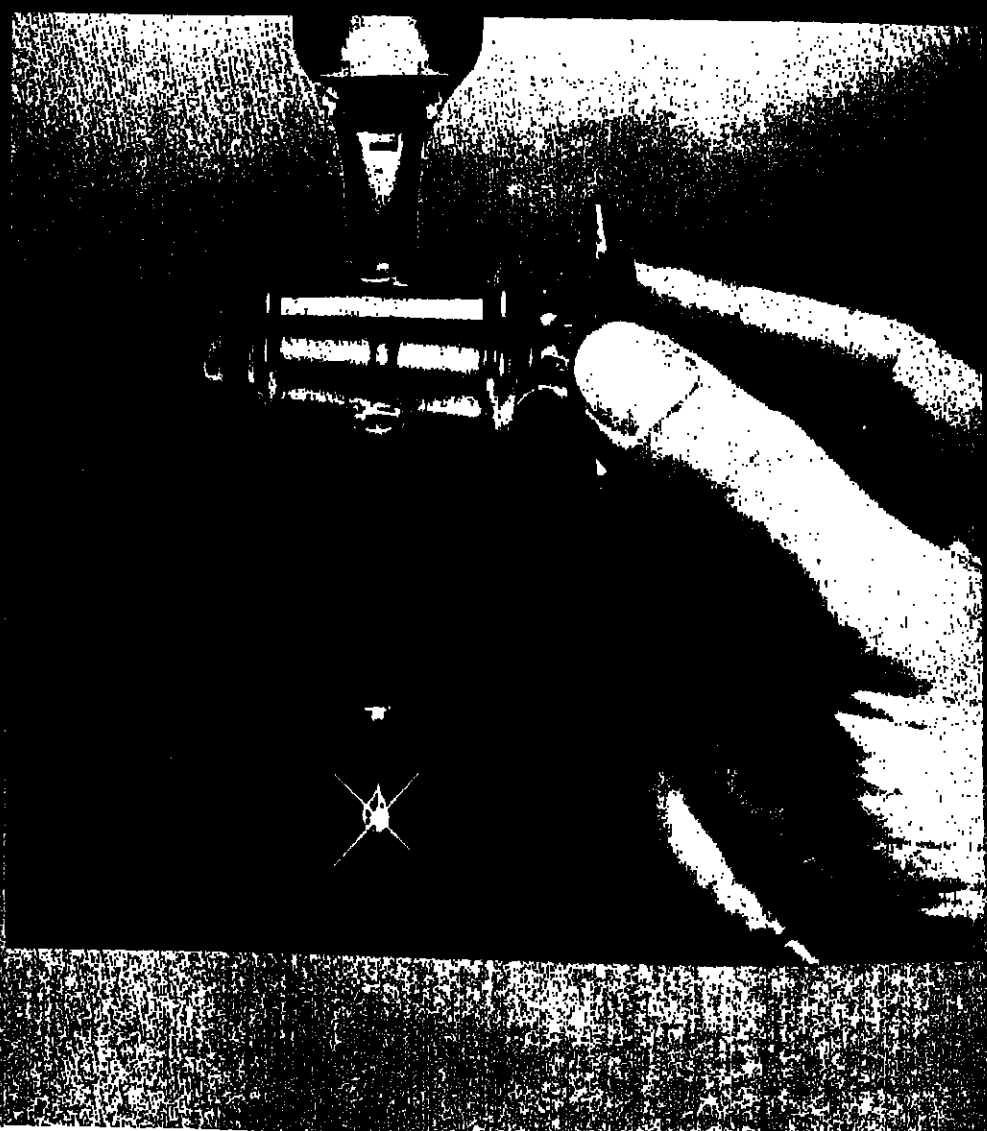
Events have demonstrated the need to have my mother admitted to a nursing home where she could receive proper attention. Although she is still active and alert, we are both concerned about the transfer of her assets to me. The current depressed economic conditions and when to do this is our problem. Is there any advantage in when you do this?

Upstate New York, M.D.

The decision depends upon the size of her holdings. If they are large enough to be taxable as an estate, they should be transferred as soon as possible because the gift tax is lower than the inheritance tax. This strategy is betting on at least two years of life expectancy. Remember that assets transferred to an heir within two years prior to the death of the owner are deemed transferred in anticipation of death and therefore are taxed to the estate, not the recipient.

The tax code offers another helpful option—buying the "flower bonds" the Treasury offers as an inducement for aging taxpayers.

Send your questions on finances, investments, taxes to Janeway, MEDICAL TRIBUNE, 880 Third Avenue, New York, N.Y. 10022.

Esimil...begins  
with a thiazide

## Esimil

guanethidine monosulfate 10 mg  
hydrochlorothiazide 25 mg

## INDICATIONS

Hypertension. (See box warning.)

**WARNING**  
This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage as determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

**CONTRAINDICATIONS**  
Guaneethidine: Known or suspected pheochromocytoma; hypersensitivity to guaneethidine; heart failure not due to hypertension; use of MAO inhibitors.  
Hydrochlorothiazide: Anuria; hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous.

**WARNINGS**  
Antihypertensives are potent drugs and can lead to disturbing and serious clinical problems. Physicians should be familiar with all uses and patients should be warned not to deviate from instructions.

## Guaneethidine

Warn patients about the potential hazard of orthostatic hypotension, which can occur frequently and is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. To help prevent fainting, warn patients to sit or lie down with onset of dizziness or weakness, which may be particularly dangerous during the initial period of dosage adjustment and with postural changes. The potential occurrence of these symptoms may require alteration of previous daily activity. Caution patients to avoid sudden or prolonged standing or exercise while taking the drug.

Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression.

If possible, withdraw therapy 2 weeks prior to surgery to reduce the possibility of vascular collapse and cardiac arrest during anesthesia. If emergency surgery is indicated, administer pre-anesthetic and anesthetic agents cautiously in reduced dosage and have oxygen, atropine, resuscitators, and IV solutions ready for use. Patients on guaneethidine should be used with extreme caution in the presence of augmented response and the greater propensity for cardiac arrhythmias.

Dosage requirements may be reduced in presence of fever. Exercise special care when treating patients with a history of bronchial asthma. Hydrochlorothiazide

Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of this drug may develop in patients with impaired renal function.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid

and electrolyte imbalance may precipitate hepatic coma.

Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs. Sensitivity reactions are more likely to occur in patients with a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

**Usage in Pregnancy**  
Guaneethidine: The safety of guaneethidine for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

**Hydrochlorothiazide:** Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

**Nursing Mothers**  
Thiazides cross the placental barrier and appear in cord blood and breast milk.

**PRECAUTIONS**  
Guaneethidine: The effects of guaneethidine are cumulative over long periods; initial dose should be small and increased gradually in small increments. Use very cautiously in hypertensive patients with a history of hypotension or renal insufficiency or recent myocardial infarction. In patients with severe cardiac failure except with extreme caution. In incipient cardiac decompensation weight gain or edema may be averted by the administration of a thiazide. Remember that both digitalis and guaneethidine slow the heart rate.

...because it is the standard initial therapy—the logical foundation upon which to build. And we picked hydrochlorothiazide, the most widely prescribed diuretic-antihypertensive, which we

...added to perhaps the most effective antihypertensive available, guanethidine...

to create a logical team of therapeutic activities ...for controlling moderate to severe hypertension.

to provide an alternative therapy ...which often controls hypertension in patients not responding to sedatives, diuretics, rauwolfia-thiazides, or other centrally acting inhibitors alone or in combination.

to avoid exacerbating the problem of mental depression ...because Esimil contains no reserpine.

to encourage patient compliance ...because Esimil usually works in once-a-day dosage.

Like all antihypertensives, Esimil should be given with caution in the presence of severe coronary insufficiency or recent myocardial infarction.

Dissatisfied with your present antihypertensive therapy? Why don't you start with the same effective components we did, and when your carefully titrated dosage matches ours—switch to Esimil.

titrate to

Esimil

guanethidine monosulfate 10 mg  
hydrochlorothiazide 25 mg

Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone.

Amphetamine-like compounds, stimulants (eg, amphetamine, methylphenidate), tricyclic antidepressants (eg, amitriptyline, imipramine, desipramine) and other psychopharmacologic agents (eg, phenothiazines and related compounds). Sensitivity reactions may reduce the hypotensive effect of guanethidine. Discontinue MAO inhibitors for at least one week before starting guanethidine.

**Hydrochlorothiazide:** Periodic determination of serum electrolytes to detect possible electrolyte imbalances should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hypotension, hypochloremic alkalosis, and hypokalemia). Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids.

Medication such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular twitching, tetany, or convulsions, paresthesias, hypokalemia, oliguria, ischuria, and anorexia.

Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver diseases or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Although a causal relationship has not been established, a few instances of anemia, thrombocytopenia and leukopenia have been reported.

In actual salt depletion, appropriate replacement is the therapy of choice.

Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.

Hypocalcemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration.

Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.

If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.

Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

**ADVERSE REACTIONS**

Guaneethidine: Frequent reactions due to sympathetic blockade—dizziness, weakness, lassitude, syncope. Frequent reactions due to unopposed parasympathetic activity—bradycardia, increase in bowel movements, diarrhea (may be severe and necessitate discontinuance of the drug). Other common reactions—fatigue, muscle cramps, mental depression, chest pains (angina), loss of appetite, dry mouth, rise in BUN, paresthesias, myalgia, muscle tremor, mental depression, chest pains (angina), or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Although a causal relationship has not been established, a few instances of anemia, thrombocytopenia and leukopenia have been reported.

**Hydrochlorothiazide:** Gastrointestinal—anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestasis), pancreatitis. Central Nervous System—dizziness, vertigo, paresthesias, headache, xanthopsia. Dermatologic—hypersensitivity—rash, urticaria, necrolytic epidermal detachment, Stevens-Johnson syndrome, and drug fever. Hematologic—other hypersensitivity reactions, thrombocytopenia, leukopenia, agranulocytosis, or thrombocytopenic purpura. Cardiovascular—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Other—hyperglycemia, glycosuria, hyperuricemia, muscle spasms, weakness, restlessness. Whenever adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

**DOSEAGE**  
As determined by individual titration (see box warning).

**HOW SUPPLIED**  
Esimil is available in 10 mg and 25 mg capsules (white, scored), each containing 10 mg guanethidine monosulfate and 25 mg hydrochlorothiazide; bottles of 100.

CIBA Pharmaceutical Company  
Division of CIBA-GEIGY Corporation  
Summit, New Jersey 07901

C I B A

First Month Held  
'Critical Period'  
In Compliance

Continued from page 7

"interferes with or alters the patient's daily pattern of living, the less likely it is to be followed." A realistic schedule, worked out with the patient himself, may be better than an "ideal" one which he may not follow, he added.

The use of calendar-dose packaging, sustained release medications, and fixed drug combinations are also helpful. For patients who still fail to take their medication, Dr. Bigger recommended having them bring their medication to the office for personal inspection.

Psychologically, noncompliant patients are typically those who show little concern for their health, who do not believe in the benefit of the therapy or the office visit, and who do not understand physician instructions, he said, adding that economic factors also play a part in this behavior.

However, the physician is responsible for noncompliance when he fails to explain the patient's situation clearly, or is hostile, argumentative, or demonstrates uncertainty regarding therapeutic efficacy, Dr. Bigger said.

To counteract these tendencies, he urged improved physician-patient relations as a general rule, a concerned and compassionate physician attitude, and clear-cut explanations to the patient.

Noncompliance in keeping appointments, Dr. Bigger said, is best handled by reviewing at the end of the day the record of patients who failed to show or cancelled without making another appointment.

"The advantages of this day-to-day recall system are that it requires little additional time, as only selected patients will need to be recalled, and the efforts are not expended on patients who will keep their appointments anyway."

## Sharks in Cancer Study



Patricia Byfield, Ph.D., U.C.L.A. Assistant Professor of Pediatrics, extracts "primitive" lymphocytes from a live shark in order to study their potential role in immune response to cancer.

# LIBRIUM® AT WORK: (chlordiazepoxide HCl)

IN THE ANXIOUS PATIENT  
WITH ORGANIC GASTROINTESTINAL  
DISEASE

## J.K.: A CASE IN POINT\*

**PATIENT:** 35-year-old male, Caucasian.

**FAMILY HISTORY:** Mother diabetic.

**MEDICAL HISTORY:** Followed as part of diabetic study since childhood 1x/year. Normal glucose tolerance tests in 1968, 1969 and 1970.

12/66 — Single episode of being awakened by nausea and vomiting, followed by slight diarrhea. Physical exam normal. Slight diffuse abdominal tenderness. Dx: gastroenteritis.

12/66-2/71 — Routine visits. Complaints of intermittent midepigastic pain; physical exams and laboratory findings normal. Appeared anxious and tense; smoked heavily; overweight (15-20 lbs). 2/68 — Librium 10 mg t.i.d.; 1200 calorie diet; advised to stop smoking. 2/71 — G.I. series; suspicion of duodenal ulcer.

9/73 — Intermittent midepigastic pain, relieved by food. G.I. series; results show spastic and irritable bulb with thickening of folds, niche visible at base of bulb. Dx: duodenal ulcer. Rx: Librium 10 mg q.i.d. to relieve anxiety; ulcer diet in four feedings; antacids.

9/74 — Infrequent episodes of midepigastic pain relieved by food. Physical and laboratory findings normal.

**PRESENT TREATMENT:** Librium 10 mg t.i.d.; p.r.n.; antacids p.r.n.; diet; routine follow-up.

**IMPRESSION:** Responding well to medical regimen — G.I. symptoms under control; anxiety and tension manageable; still smokes.

\*Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley, New Jersey. Although this is an actual case history, not all cases can be expected to have the same response to therapy.

## CLINICAL ANXIETY AND THE G.I. PATIENT

After the ulcer patient's acute episode is under control, your counseling and reassurance about the status of the ulcer are often enough to allay anxiety. In some patients, however, excessive anxiety and emotional tension may interfere with medical management. When this occurs, Librium (chlordiazepoxide HCl) may be a beneficial adjunct.

Librium offers a high degree of antianxiety effectiveness, with relatively few side effects, for the ulcer patient. In addition to a long clinical record of prompt and effective action, Librium has an established safety record and an excellent record of patient acceptance. In proper dosage, it usually helps calm the overanxious patient without interfering with mental acuity or general performance. However, as with all CNS-acting drugs, patients should be cautioned against hazardous activities requiring complete mental alertness. Librium is often used concomitantly with certain specific medications of other classes of drugs, e.g., anticholinergics and antacids. Of course, Librium therapy should be discontinued after anxiety has been reduced to tolerable levels.

WHEN CLINICAL ANXIETY INTERFERES  
WITH PATIENT MANAGEMENT

**LIBRIUM®**  
chlordiazepoxide HCl/Roche  
5 mg, 10 mg, 25 mg capsules  
FOR ALL THE RIGHT REASONS

Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** Relief of anxiety and tension occurring alone or accompanying various disease states.

**Contraindications:** Patients with known hypersensitivity to the drug.

**Warnings:** Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation or in women of child-bearing age requires that its potential benefits be weighed against its possible hazards.

**Precautions:** In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

**Adverse Reactions:** Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido — all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

**Supplied:** Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110



## HEW Considering Network of Centers for Amniocentesis

Continued from page 1

mester amniocentesis in more than 1,000 women, were described by clinical investigators and N.I.C.H.D. officials during a symposium held at the annual meeting of the American Academy of Pediatrics.

Dr. Theodore Cooper, Assistant Secretary for Health in the Department of Health, Education, and Welfare, told the symposium that "We can now say with virtual certainty" that this technique is safe and "can be applied to larger segments of the population without undue risk or hazard."

In a statement expected to have major impact, Dr. Cooper further declared:

"It is most appropriate for the Public Health Service, as a matter of policy, to foster use of amniocentesis by those women for whom it is indicated by educating both physicians and the public as to the availability and applicability of the technique and, based on results of this study, its safety."

### PHS To Act

Attempts will be made by the Public Health Service to assure coverage for the procedure by both the private and the public medical insurance programs, he said.

The study compared the outcome of pregnancy in 1,040 women who had amniocentesis performed and in 992 matched controls who had no condition indicating a need for the procedure or who had refused it. Nine medical centers participated in gathering data for the collaborative project, which started in June, 1971, and was completed in June, 1975.

Since the primary purpose was to determine whether or not amniocentesis for prenatal diagnosis has adverse effects on the pregnant women or the fetus, the following findings were stressed in the evaluations:

- The rate of fetal loss from spontaneous abortion or stillbirth for the amniocentesis group was 3.5 per cent compared with 3.2 per cent for the controls—a statistically insignificant difference.
- Examinations of newborns showed no evidence of fetal injury that could be attributed to amniocentesis.
- A comparison of the infants born to control women and to women who had undergone amniocentesis revealed no significant difference in the incidence of congenital anomalies not detectable by amniocentesis.
- Follow-up testing of both groups of infants (primarily at ages 11 to 13 months) showed no significant differences between them as far as growth and developmental status were concerned, or in the incidence of physical or neurologic abnormalities.

Among the 1,040 women undergoing a total of 1,195 taps, 11 experienced vaginal bleeding and there were other relatively minor complications but no significant differences were observed between control and test women in complications of pregnancy, labor, or delivery. The rate of prematurity was essentially the same in both groups.

The great majority of the procedures (91.3 per cent) were performed for

cytogenetic indications. Approximately half of these were done in women aged 35 or older. The remaining 8.7 per cent of the procedures were performed for detection of metabolic disorders.

### Abortion Elected

A total of 19 chromosomally abnormal fetuses and 15 fetuses with metabolic disorders were identified. Additionally, 11 male fetuses were identified as having a 50 per cent risk of x-linked disorders such as hemophilia and Duchenne's muscular dystrophy.

Abortion was elected by 39 of the 45 women with fetuses at risk. Eight of the abortions proved to have Down's syndrome, as did seven infants born to women in the control group.

Only six errors in prenatal diagnosis occurred, for an overall accuracy of better than 99 per cent. In three instances, the sex was misidentified (although not in tests specifically performed to determine sex), and in one case galactosemia was wrongly suspected in a fetus proving normal at birth. The errors considered serious were the failures to diagnose Down's syndrome in two fetuses.

Many of the investigators speaking at the symposium emphasized that the high levels of safety and accuracy shown in the study were achieved by experienced scientists working in well-equipped medical centers.

Dr. Cooper's statement called attention to the fact that "the limiting factor in expanding amniocentesis" is likely to be the availability of good laboratory facilities, noting that nearly all the analyses of amniotic fluids currently done in this country are performed in research laboratories where work has been supported by research grants.

This arrangement will not be feasible as amniocentesis becomes an accepted clinical practice, he pointed out, and therefore he believes "government involvement is probably necessary and appropriate" in gearing up a nationwide analysis capability.

### Two Approaches

Two approaches are currently being considered by Dr. Cooper. One would be for the Public Health Service to establish a network of state or regional laboratories to perform the cytogenetic analyses, with research labs continuing to provide facilities for biochemical analyses.

The government, Dr. Cooper said, would provide "seed money" for space, equipment, and training of personnel at network facilities, which "ideally" would be established at pre-existing university centers.

Another alternative under consideration is to establish a "nationwide analysis capability under the aegis of the Center for Disease Control," to work with state and local institutions.

"In fact, a pilot project, in collaboration with a state health department and university, is already underway," Dr. Cooper said.

The centers participating in the N.I.C.H.D.-sponsored study were Children's Memorial Hospital (Chicago); Eunice Kennedy Shriver Center

## For Education In Cardiovascular Disease



Groundbreaking ceremonies for "Heart House" were held by American College of Cardiology in Bethesda, Md., where new facility will contain the College's headquarters and serve as a national center for the continuing education of physicians and other scientists concerned with cardiovascular diseases. It is intended to supplement regional facilities and supply a centralized source for accumulation and dissemination of research findings. Participants in ceremony are (l. to r.) Sen. J. Glenn Beall (R-Md.), former ACC president Dr. B. L. Martz, Rep. Gilbert Gude (R-Md.), and Sen. Charles Mathias (R-Md.).

(Boston); Johns Hopkins University School of Medicine; Mt. Sinai School of Medicine; University of California at Los Angeles (Harbor General Hospital); University of California (San Diego)

School of Medicine; University of Michigan School of Medicine; University of Pennsylvania School of Medicine; and Yale University School of Medicine.

## Ultrasonic Visualization Aids Differentiation of Jaundice

Medical Tribune Report

WINSTON-SALEM, N.C.—Ultrasonic visualization of dilated common bile ducts and biliary radicles is a safe and sensitive, noninvasive method of differentiating obstructive from nonobstructive jaundice, two Pennsylvania investigators told the 20th Annual Conference of the American Institute of Ultrasound in Medicine.

It is in fact the method of choice in imaging the biliary tract in jaundiced patients since noninvasive radiographic techniques result in insufficient opacification of the tract, according to Dr. Gordon S. Perlmutter of the Reading Hospital and Medical Center in Reading, Pa., and Dr. Barry B. Goldberg, Professor of Radiology at Temple University in Philadelphia.

Ultrasonography cannot, however, determine the etiology of the obstruction. But this is a minor drawback, explained Drs. Perlmutter and Goldberg, "since surgery is indicated in almost all cases of obstructive jaundice."

### Linear Scan

In a six-month interval, 44 patients with jaundice were scanned on a commercially available gray scale unit which included a scan converter and TV display. "All scans were performed with a simple linear scanning technique with a minimum of sectoring and overwriting," the radiologists said.

In 16 cases, obstructive or extrahepatic jaundice was identified by the presence of dilatation of the biliary tract. Seven patients had recognizable dilatation of the common bile duct

while the other nine were diagnosed on the basis of an enlarged gall bladder and dilated intrahepatic ducts.

"All cases diagnosed as having obstructive jaundice at ultrasonography were proven at surgery to have a mechanical obstruction," the investigators said. But "the cause of obstruction could only be reliably determined preoperatively in two cases with demonstrable common duct stones."

The radiologists warn that "great care is mandatory in performing and interpreting ultrasonograms," since portal and biliary structures may be confused. "It is necessary to establish the continuity of the dilated intrahepatic radicles with the common duct before the diagnosis of an enlarged common bile duct can be accurately made."

"In our experience, if the common bile duct is visualized at ultrasonography, it has been larger than 8 mm and therefore dilated. Only one exception to this has occurred to date, where a 6 mm common bile duct was visualized in a normal patient."

## Inhospital Electroconvulsions

Medical Tribune Report

CHICAGO—A nationwide search for incidents of accidental electroconvulsions in hospitals, conducted by correspondence and personal observation, did not "yield any evidence to support the contention that there has been wholesale injury and death as a result of faulty electrical devices," Dr. John M.R. Bruner, of Harvard Medical School, told the American Society of Anesthesiologists.



## What a difference a day can make

Your counsel and reassurance—and Ritalin.

A logical first step in treating mild depression, and often all that's needed to bring quick symptomatic relief.

Indeed, your patient may be-

gin to feel better within hours—her spirits boosted, her mood brightened. A single prescription may be all that's needed.

Ritalin is usually well tolerated even by older or convalescent patients. Note, however,

that it is not indicated in the more severe depressions. But whenever depression is mild, think of Ritalin—so your patient has a better chance of waking up to a brighter tomorrow.

**Ritalin**  
(methylphenidate)  
acts quickly to relieve symptoms  
in mild depression

\*This drug has been evaluated as possibly effective for this indication. See brief prescribing information.

Ritalin® hydrochloride (C)  
(methylphenidate hydrochloride)  
TABLETS

**INDICATION**  
Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indication as follows:  
"Possibly" effective: Mild depression  
Final classification of the less-than-effective indications requires further investigation.

**CONTRAINDICATIONS**  
Marked anxiety, tension, and agitation, since Ritalin may aggravate these symptoms. Also contraindicated in patients known to be hypersensitive to the drug and in patients with glaucoma.

**WARNINGS**  
Ritalin should not be used in children under six years, since safety and efficacy in this age group have not been established. Sufficient data on safety and efficacy of long-term use of Ritalin in children with minimal brain dysfunction are not yet available. Although a causal relationship has not been established, suppression of growth (ie, weight gain and/or height) has been reported with long-term use of stimulants in children. Therefore, children requiring long-term therapy should be carefully monitored.

Ritalin should not be used for severe depression of either exogenous or endogenous origin or for the prevention of normal fatigue states. Ritalin may lower the convulsive threshold in patients with or without prior seizures; with or without prior EEG abnormalities, even in absence of seizures. Safe concomitant use of anticonvulsants and Ritalin has not been established. If seizures occur, Ritalin should be discontinued. Use cautiously in patients with hypertension. Blood pressure should be monitored at appropriate intervals in all patients taking Ritalin, especially those with hypertension.

**Drug Interactions**  
Ritalin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents and MAO inhibitors. Ritalin may inhibit the metabolism of coumarin anticoagulants, the metabolism of phenothiazines, diphenhydramine, imipramine, phenylbutazone, and tricyclic antidepressants (nortriptyline, desipramine). Downward dosage adjustment of these drugs may be required when given concomitantly with Ritalin.

**Usage in Pregnancy**  
Adequate animal reproduction studies to establish safe use of Ritalin during pregnancy have not been conducted. Therefore, until more information is available, Ritalin should not be given to women of childbearing age unless, in the opinion of the physician, the potential benefits outweigh the possible risks.

**Drug Dependence**  
Ritalin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may increase dosage on their own initiative. Chronically abusive use can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal, since severe depression as well as the effects of chronic overactivity can be unmasked. Long-term follow-up may be required because of the patient's basic personality disturbances.

**PRECAUTIONS**  
Patients with an element of agitation may react adversely; discontinue therapy if necessary. Periodic CBC, differential, and platelet counts are advised during prolonged therapy.

**ADVERSE REACTIONS**  
Nervousness and insomnia are the most common adverse reactions but are usually controlled by altering the dose and omitting the drug in the afternoon or evening. Other reactions include: hyperactivity (including skin rash, urticaria, hives, and other allergic manifestations); anorexia; weight loss; dizziness; palpitations; headache; dry mouth; constipation; abdominal pain; nausea; vomiting; diarrhea; urinary retention; tachycardia; angina; cardiac arrhythmias; abnormal electrocardiogram; prolonged QT interval; in children, loss of appetite, abdominal pain, weight loss during prolonged therapy. In some patients, a causal relationship has not been established. The following have been reported in patients taking this drug: leukopenia and/or anemia; a few instances of scalp hair loss. In children, loss of appetite, abdominal pain, weight loss during prolonged therapy. In some patients, a causal relationship has not been established. The following have been reported in patients taking this drug: leukopenia and/or anemia; a few instances of scalp hair loss. In children, loss of appetite, abdominal pain, weight loss during prolonged therapy.

**DOSEAGE AND ADMINISTRATION**  
Adults: Administer orally in divided doses 2 or 3 times daily, preferably 30 to 45 minutes before meals. Dosage will depend upon indication and individual response.

Average dosage is 20 to 30 mg daily. Some patients may require 40 to 60 mg daily. In others, 10 to 15 mg daily will be adequate. The few patients who are unable to sleep if medication is taken late in the day should take the last dose before 6 p.m.

**HOW SUPPLIED**  
Tablets, 20 mg (pale green, scored); bottles of 100 and 1,000.

Tablets, 10 mg (pale green, scored); bottles of 100, 500, 1,000 and Accu-Pak blister units of 100, 500, 1,000.

Tablets, 5 mg (pale yellow); bottles of 100, 500 and 1,000.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company  
Division of CIBA-GEIGY Corporation  
Summit, New Jersey 07901

C I B A

